T H E S I S

Submitted for the DEGREE of M.D., EDINBURGH UNIVERSITY

entitled

"THE INCIDENCE, SYMPTOMATOLOGY, DIAGNOSIS, PROGNOSIS and TREATMENT of GONOCOCCAL ARTHRITIS",

BY

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Since the discovery of the gonococcus by NEISSER[1] in 1879, and its isolation by BUMM[2] in 1885, the entire medical conception of gonorrhoea has changed, and the gonococcus has become known as one of the most important of the pathogenic bacteria.

What was once regarded as a trivial ailment is recognised today as a serious infectious disease; an infection which, although readily amenable in its earliest stages to prompt and thorough treatment, is capable, if allowed to proceed unchecked, of producing extensive inflammatory changes, not only locally, by direct and lymphatic spread throughout the tissues of the genito-urinary system, but also by way of the blood-stream, in practically any part of the body.

CUSHING[3] in 1899, referring to the gonococcus said, "Few organisms, not even the bacillus "typhosis, rival it in the number of suppurative "sequelae which may follow a primary infection. Its "occurrence in the conjunctivae, and in the iris, "the bones, the joints, bursae, and tendon sheaths, "its occasional demonstration as the cause of endo- "carditis and pericarditis, pleuritis and phlebitis, "and the recent observations of the blood, show that "its/

"its possibilities for metastatic complications are "as numerous as are those arising from spread by "direct continuity of surfaces".

The commonest manifestation of metastatic gonorrhoea is arthritis. As early as 1781 it was described by SALLE and SWEDIAUR (4) as "an inflammatory articular affection dependent upon gonorrhoea", and SIR BENJAMIN BRODIE (5) in 1818, described in detail five undoubted cases of gonococcal arthritis. At this period, however, gonorrhoea and syphilis were regarded as the same disease, the former a special or mild variety of the latter. This view was universally held until 1832, when RICORD (6) in Paris, demonstrated by a series of comprehensive experiments, that these diseases were distinct entities, each with its own virus.

INCIDENCE.

SIR WILLIAM OSLER (7) has described arthritis as the most damaging, disabling, and serious complication of gonorrhoea. He states that it occurs in 2-5% of all cases.

In a series of 3,000 consecutive male cases of/

of gonorrhoea treated in the Venereal Diseases Department of the Royal Infirmary, Edinburgh, I found 95 cases of arthritis, or 3·16%.

POLLOCK and HARRISON,(8) in a study of 812 cases of gonorrhoea in the British Army, observed arthritis in only 1·85%.

IRELAND(9) in a review of the U,S. Army Medical Records from 1st April 1917, to December 31st 1919, found 7·895 cases of gonococcal arthritis, in 259,899 admissions on account of gonococcal infection, or 3·03%.

KLOSE (1919)(10) states that before the Great War in Germany the incidence of gonococcal arthritis was 2%. During the War it was 10%, due, he considers, to improper treatment of urethral gonorrhoea, and weakened physical condition of the patients.

The number and percentage, of the various complications that occurred in 3000 consecutive cases of Anterior Urethritis of gonococcal origin in the male, are shown in TABLE I.

TABLE/

TABLE I.

	Cases.	Percentage.
Anterior Urethritis	3000	100%
Posterior Urethritis	2414	80•46
Prostatitis	673	22•43
Prostatitis and Vesiculitis	1071	35•70
Prostatitis Total	1744	58•13
Epididymitis Right	174	5•80)12•5 unilateral
" Left	191	6•70)
" Bilateral	29	0•96
" Total	294	13•46
Cowperitis	14	0•46
Periurethral Abscess	20	0•66
Parameatal duct infection	3	0•10
Tyson's duct infection	9	0•30
Ophthalmia	4	0•13
Iritis	2	0•06
Toxic conjunctivitis	3	0•10
Inguinal "bubo"	1	0•03
Hyperkeratosis Blenorrhagica	1	0•03
ANTHRITIS	95	3•16%

It is generally acknowledged that gonococcal arthritis is more common in men, than in women. In 934 successive cases of gonorrhoea in adult women, attending the Royal Infirmary, Edinburgh, I found 18 cases, or 1.92%.

TABLE II. which includes juvenile cases also treated, shows the number and percentage of complications.

TABLE II.

PARTS INVOLVED.	NO. of CASES.	PERCENTAGES.	
Urethra alone.	274	29·3	
Cervix alone.	161	17·2	
Both Cervix & Urethra.	499	53·4	
Total Urethra & Cervix.	934	100·0	
UTERINE TUBES.			
Right side.	27	2·9	Total adult cases 934.
Left side.	16	1·7	
Both sides.	8	·8	
Total.	51	5·4	
BARTHOLINIAN GLANDS.			
Right side.	143	15·3	
Left side.	99	10·6	
Both sides.	36	3·9	
Total.	278	29·8	
SKENE'S DUCT.	4	·4	Percentage of Arthritis =1·92
CONJUNCTIVA.			
Unilateral	2	·2	
Bilateral	2	·2	
JOINTS.	18	1·92	
OPHTHALMIA NEONATORUM			
Unilateral	5		Total cases in children 66 (No cases of Arthritis)
Bilateral	10		
Total	15		
VULVO-VAGINITIS.	51		

OSLER (11) quotes COLE, who in one series of cases of gonococcal arthritis at the Johns Hopkins Hospital, encountered 43 male, and only 7 female cases, and in a series of 253 cases collected by WORTHRUP, and quoted by the same author, 230 were in males.

THOMAS, (12) Philadelphia, in a series of 107 cases, found males to be more frequently affected than females, in the proportion of 97 to 10, and states that this is probably due to the fact that males possess seminal vesicles and a prostate, and a more complicated, longer and poorly draining urethra.

In a series of 84 cases of gonorrhoea in adult women, treated in East Pilton Hospital, I found arthritis as a complication in 6 cases, a percentage of 7.1. As the patients admitted to the venereal wards of this hospital are recommended from other treatment centres in Edinburgh, this high incidence is easily explained. Of the 119 cases of gonococcal arthritis I have studied, 95 are male, and 24 female cases.

The number and percentage of complications occurring in the Pilton Hospital Series, is given in the following TABLE.

TABLE III.

PARTS INVOLVED.		NO. of CASES.	PERCENTAGE.	
Urethra alone.		10	11·9	
Cervix alone.		5	5·9	
Urethra & Cervix together.		69	82·2	
Total.		84	100·0	
BARTHOLINIAN GLAND.				
"	Right	2	2·3	
"	Left	1	1·3	
"	Both	4	4·6	
	Total	7	8·2	
UTERINE TUBES.				
" "	Right	7	8·2	
" "	Left	2	2·3	
" "	Both	4	4·6	
	Total	13	15·1	
JOINTS		6	7·1	
OPHTHALMIA NEONATORUM.				
Unilateral		5		No cases of Arthritis.
Bilateral		32		
Total		37		
VULVO-VAGINITIS		37		

A G E .

In the series of 95 cases of gonococcal arthritis in adult males, the ages ranged from 20 to 53 years. Arthritis may complicate gonorrhoea at any age, but it is more frequently met with between the ages of 20 and 40. The number and percentage of cases occurring in four age periods in men, are shown in the following TABLE.

TABLE IV.

AGES.	CASES	PERCENTAGES.
Between 20-30	43	45.3
30-40	32	35.7
40-50	15	15.8
Over 50	5	5.3

In the female cases the ages ranged from 18 to 50, and the incidence of gonococcal arthritis was highest between the ages of 18 and 30, as shown in TABLE V.

TABLE V.

AGES.	CASES	PERCENTAGES.
Between 18-20	6	33.3
20-30	6	33.3
30-40	1	5.5
40-50	5	27.7

The majority of cases of gonococcal arthritis occur in adults. Occasionally, however, arthritis complicates gonococcal conjunctivitis in infants, and vulvo-vaginitis in young girls. McDONAGH (13) states that it is not at all uncommon in cases of vulvo-vaginitis.

In a review of 37 cases of ophthalmia neonatorum, and 37 cases of vulvo-vaginitis in East Pilton Hospital, and 15 cases of ophthalmia, and 51 cases of vulvo-vaginitis in the Royal Infirmary, Edinburgh, I was unable to find a single case of arthritis as a complication.

JOINT INVOLVEMENT.

As a rule more than one joint is affected. In the 95 male cases, the arthritis was monarticular in 15 cases or 15.8%, and in 80 cases or 84.2%, two or more joints were involved.

Commencing usually in one joint, the inflammation soon appears in other joints, and in the course of a few days there may be widespread articular involvement. During this time symptoms persist in the earlier joints affected.

Although practically any joint in the body may be affected, certain joints are more often involved.

In the male cases under review the joints affected/

affected were the knee, ankle, metatarso-phalangeal, shoulder, wrist, metacarpo-phalangeal, elbow, hip, spine, and mandibular in order of frequency. TABLE VI. shows the relative frequency of involvement of the various joints.

TABLE/

TABLE VI.

JOINT.	RIGHT.	LEFT.	TOTAL UNILATERAL.	TOTAL BILATERAL.	TOTAL.	PERCENTAGE.
Knee	17	20	37	24	61	64·2
Ankle	10	10	20	15	35	36·8
Meta-tarso-phalangeal	14	9	23	10	33	34·7
Shoulder	8	5	13	9	22	23·1
Wrist	8	3	11	3	14	14·7
Meta-carpo-phalangeal	8	1	9	4	13	13·6
Elbow	4	5	9	2	11	11·5
Hip	1	3	4	-	4	4·2
Spine	- 3	-	-	-	3	3·1
Mandibular			2	-	2	2·1

Arthritis may arise during the acute, subacute, or chronic stages of gonorrhoea. In two cases in my series it became evident five days after the appearance of the urethritis. This was the shortest interval that elapsed between the onset of urethral symptoms, and the development of arthritis; the longest was 15 weeks.

Cases are not infrequently met with in which the gonococci have remained latent in the prostate and seminal vesicles for years, before giving rise to metastatic complications. KIDD (14) (1923), reports cases of arthritis which commenced 13, 25, and 44 years after the primary attack of gonorrhoea, - and BEZANCON, WEIL & RUBINSTEIN (15) (1925) quote cases in which the gonococci had remained dormant in the prostate and vesicles for 5, 7, and 24 years, before giving rise to metastatic joint envolvement.

Occurring in the acute stage of a gonococcal infection, arthritis usually manifests itself in the second or third week. In the series under review, 16% of cases commenced in the first seven days, 55% in the first fifteen days, 67% in the first twenty-five days, and 80 % the first twenty-eight days. TABLE VII. shows the interval elapsing between the onset/

onset of the urethritis, and the commencement of arthritis in 62 cases.

TABLE VII.

INTERVAL between ONSET of URETHRITIS & ONSET of ARTHRITIS.	NO. of CASES.	
5 days	2	
7 "	8	
8 "	2	16% in 1st 7 days
10 "	3	
11 "	1	
2 weeks	14	
2½ "	2	55% in 1st 15 days
3 "	5	
3½ "	2	
4 "	7	
5 "	2	67% in 1st 25 days
7 "	3	
8 "	1	
11 "	3	
12 "	2	80% in 1st 48 days
15 "	1	
	62	

An/

An arthritis may complicate a first attack of gonorrhoea, but it frequently commences during the first, second, or later reinfections, or during recurrences of the uncured original attack. In the 95 male cases 50 or 52.4% followed the first attack, 43 or 45.2% the second, and 2 or 2.1% the third attack.

If a person who has suffered from gonococcal arthritis and been cured, acquires gonorrhoea at a later date, arthritis is very liable to reoccur and previously infected joints seem especially prone to reinfection - a condition of affairs pathognomonic of gonococcal arthritis (McDONAGH)(16). This is more often the case with the larger joints, the smaller joints of the hands and feet showing less tendency to become reinfected.

AETIOLOGY.

Arthritis is always a metastatic complication and never a primary manifestation of gonorrhoea. In the adult the primary focus of infection is in the genito-urinary system, some parts of which are more liable to harbour gonococci and give rise to blood-borne dissemination than others.

In/

In men involvement of the posterior urethra with infection of the prostate and vesicles, is present in the vast majority of such cases. In the 95 male cases observed in this series, the posterior urethra was affected in every case, and there was evidence of prostatic infection in 90.3%; the seminal vesicles were diseased in 54.3%. The various complications of gonorrhoea occurring in these cases, are recorded in TABLE VIII.

TABLE/

TABLE VIII.

Showing number and percentage of complications of gonorrhoea occurring in 95 cases of gonococcal Arthritis.

COMPLICATIONS.	NO. of CASES.	PERCENTAGE.
Posterior Urethritis.	95	100
Prostatitis.	36	37·9
Combined Prostatitis, & Vesiculitis.	50	52·4
Vesiculitis.	2	2·1
Periurethral Abscess	1	1·05
Stricture with retention	1	1·05
Toxic Conjunctivitis.	2	2·1
Exostosis of OS. Calcaneum.	4	4·2
Recurrent Iritis.	1	1·05
Hyperkeratosis Blenorrhagica.	1	1·05
Epididymitis Unilateral.	3	3·1
" Bilateral.	2	2·1
Total	5	5·2

Prostate and Vesicles were both unaffected in 9 cases (9·4%)

Although the focus of infection responsible for the majority of metastatic sequelae of gonorrhoea, is to be found in the posterior urethra, prostate; and seminal vesicles, disease of the anterior urethra, with its complications, littritis, lacunitis and submucous infiltrations, and abscesses, occasionally gives rise to arthritis. In 33 cases of gonococcal arthritis examined by MICHEL (17) (1919) infection of the anterior urethra alone was present in 12 cases without any involvement of the posterior urethra, prostate or vesicles.

In women, metastatic arthritis usually follows gonococcal infection of the urethra, Bartholinian glands, cervix uteri and uterine tubes. In 18 cases of gonococcal arthritis, the urethra was infected in 13 cases (72.2%), and the cervix in 14 cases (77.7%); one case (5.5%) had involvement of a uterine tube, and 7 cases (38.8%) had Bartholinian infection. TABLE IX. shows the number and percentage of complications of gonorrhoea occurring in 18 cases in which arthritis was present.

TABLE/

TABLE IX.

COMPLICATIONS.	NO. of CASES.	PERCENTAGE.
Urethra alone.	2	11·1
Cervix alone.	3	16·6
Urethra & Cervix together.	11	61·6
ASSOCIATED INFECTION OF BARTHOLINIAN GLANDS.		
Right	3	16·6
Left	4	22·2
Total	7	38·8
Right Uterine Tube.	1	5·5
Exostosis of OS. Calcaneum.	1	5·5

The gonococci are carried from the primary gonococcal lesion in the tissues of the genito-urinary tract, via the lymphatics to the bloodstream, and thence to the joints. The presence of the organisms in the lymphatic system was first demonstrated by COLUMBINI (18) in 1898, and two years later by UYSING (19) and others, and WERTHEIM (20) in 1896 was the first to isolate the gonococcus from the blood.

In the past there has been much discussion as to whether gonococcal arthritis was actually due to an organismal infection of the affected joints, or to a toxin of the gononoccus absorbed from disease elsewhere in the body. Certain observers held the latter view because they repeatedly failed to demonstrate the gonococcus in the aspirated synovial fluid either by film preparation or by culture.

According to NASSE and RINDFLEISCH (21) (1897), and also BAUR (22) (1901), the gonococcus can be cultivated from the affected joints in about two-thirds of the cases, if suitable technique is adopted. NASSE and RINDFLEISCH, obtained pure cultures/

cultures from the joints in 19 out of 30 cases of gonococcal arthritis, and BAUR in 19 out of 27 cases.

For the first few days after the onset of arthritis, depending on such factors as the virulence of the infection and the vital resistance of the patient, the gonococci are present in the intra-articular exudate; but they soon become limited to the synovial membranes, cartilages, or epiphyses of the bones, and the inflammatory reaction thus set up gives rise to a serous effusion into the joint, which is usually sterile on culture.

BAUR found it impossible to obtain positive cultures of gonococci from the joint fluid later than the 6th day after the onset of the arthritis.

In 9 cases of gonococcal arthritis examined by Mc DONAGH (23) the fluid obtained by joint-puncture was sterile.

THOMSON (24) (1923) has been able to cultivate the organism from the joint fluid in some ten cases of gonococcal arthritis. He emphasizes the importance of using a good culture medium and incubating for at least ten days. On two occasions in/

in his experience the colonies did not develop until the seventh day, and on a third occasion not until the tenth day.

As a rule the gonococcus is the only micro-organism found in the fluid aspirated from the joints; superadded infection with staphlococci, streptococci, and other pyogenic bacteria is uncommon. It is rare also for other organisms to be isolated alone without the gonococcus. Of BAUR'S cases only one showed mixed infection, the organism associated being a staphlococcus.

NASSE and RINDFLEISCH also held the view that mixed infection played little part in the disease.

In those cases investigated and quoted by THOMSON the cultures were pure in each instance.

AETIOLOGY IN INFANTS AND YOUNG CHILDREN.

The gonococcus may be the cause of arthritis occurring in infants and young girls. In the former the conjunctiva is primarily infected, and in the latter the vulva and vagina. In some of the latter cases there is a concomitant urethritis.

Arthritis is not a common complication of these/

these lesions, but it does occasionally occur. In each case the infection is bloodborne. In 1885 CLEMENT LUCAS[25] drew attention to an original observation of his, that the "purulent ophthalmia of new born infants, was liable in certain instances to produce inflammation of joints similar to gonococcal rheumatism in adults," and he published clinical records of three cases.

DARIER in 1889[26] demonstrated the gonococcus in the discharge from a case of suspected gonococcal conjunctivitis, and in 1890 the chain of evidence supporting LUCAS' observations was completed by DEUTSCHMANN[27] who isolated the organism from the fluid aspirated from the inflamed knee of an infant of three weeks suffering from purulent ophthalmia.

Following LUCAS' statement other clinicians observed similar cases, and by 1899 twenty-three cases had been recorded, the diagnosis being made in each instance by the demonstration of the gonococcus.

Since that date numerous cases of arthritis/

arthritis following gonococcal conjunctivitis have been reported, the more recent ones by JOHNSTONE (28) (1921) PRITZI (29) (1924) FISCHER (30) (1924) and GERTRUDE HERZFELD (31) (1925).

In the American Journal of Diseases of Children Vol.III 1927, reference is made to infection of the rectum as the primary lesion responsible for gonococcal arthritis in infants. As a result of an outbreak of gonorrhoea in a children's hospital 67 out of 182 new-born infants were infected. Of these 53 presented joint complications. The rectum was regarded as the portal of entry because a number of cases had purulent rectal discharges, ischio-rectal abscesses, and positive rectal smears.

CLINICAL/

CLINICAL FEATURES.

As OSLER (32) has pointed out variability and obstinacy, are the two most distinguishing features. This variability in the clinical appearance of gonococcal arthritis is to a large extent dependent on the virulence of the gonococcus when it reaches the joint. If during the acute stage of a urethritis gonococci gain access to an articulation the resulting inflammation will be correspondingly severe, but if the joint becomes infected with an attenuated strain of gonococci derived from an old-standing, or hitherto quiescent focus, the arthritis supervening will run a chronic course. Gonococcal arthritis thus affords an excellent example of the varying reactions of the tissues to an irritant that varies in strength.

The inflammation following a mild irritant may manifest itself clinically by arthritis pains without any of the physical signs of inflammation such as heat or redness. This condition of gonococcal/

coccal ARTHRALGIA usually affects a number of joints and the pain tends to move from joint to joint. As a rule it is a trifling and evanescent complication lasting only a few hours or a day or so, but in some cases when the primary lesion is not responding to therapeutic measures the arthralgia may persist for a longer time. The pain and stiffness are usually more marked in the morning, tending to disappear when the patient walks about.

When the virulence of the bacterial irritant is greater, one or more joints may become the seat of an ACUTE ARTHRITIS, either suddenly, or following on an initial diffuse arthralgia. The affected joints become intensely painful and swollen, the temperature rises to about 102.2 Fah., and there is considerable disturbance of general health. The skin surface of the joint is hot, tense, œdematous and red, and the slightest movement or palpation of the joint elicits pain. A serofibrinous exudate into the cavity of the joint and into the periarticular tissues accounts for the swelling. Sometimes there is little increase in the joint fluid, the swelling/

swelling being almost entirely periarticular; the capsule, and tendon sheaths surrounding the joint are thickened and oedematous, and readily palpable.

With suitable treatment resolution is the rule, but if the inflammation is allowed to proceed unchecked the fibrinous exudate slowly subsides with the formation of adhesions, both intra- and peri-articular, and deformities with grave functional disability result. Suppuration is rare in acute gonococcal arthritis. When it does occur it is a disastrous and not infrequently fatal, complication. The articular cartilages are destroyed, the ends of the bones are covered with granulations, extra-articular abscesses form, and if the patient survives, bony ankylosis is all that can be hoped for. In most cases suppuration results from superadded pyogenic infection, but gonococci alone, if the infection is sufficiently virulent, may give rise to a pyarthrosis.

When the small joints of the hands and feet are affected, redness and swelling although present are not so evident as in the larger articul-

ations/

ations and suppuration is very uncommon.

Some authors including Mc DONAGH (33) divide acute arthritis of gonococcal origin into two groups; ARTHRITIS SEROFIBRINOSA, the commonest form, in which the synovial membrane and capsule are thickened, and the joint cavity distended with a serofibrinous exudate, and PHLEGMONOUS (König), or PSEUDOMEMBRANOUS ARTHRITIS, in which the inflammation is most acute in the capsule and periarticular structures, and although there is considerable swelling, the amount of fluid in the joint is small. In the latter variety the inflammation quickly spreads to the interior of the joint, and in the case of the knee internal ligaments are liable to be destroyed with permanent subluxation of the joint.

There are two forms of chronic gonococcal arthritis:-

(i) Hydrops articuli
(ii) Osteo-arthritis

A hydrarthrosis is the result of a mild gonococcal infection resulting in a subacute synovitis, with swelling as the main clinical feature/

feature. There is almost complete absence of pain on palpation or movement, or when the joint is at rest; movements are free unless limited to a slight extent by the size of the effusion. As a rule one large joint, most often the knee, is affected, and in some cases the condition is bilateral. The onset is usually sudden. The fluid may be absorbed in the course of a day or so, but usually persists for two or three weeks or longer, and recurrences are not uncommon. A large effusion, persisting for some time, produces laxity, and later some destruction of the joint ligaments.

Chronic osteo-arthritis of gonococcal origin is the result of a low grade infection. The onset is gradual. At first a number of joints including some of the smaller joints are involved, but the majority of these clear up, the condition usually remaining and advancing in two or more larger joints. There is considerable swelling from periarticular oedema with little or no effusion in the cavity of the joint. In cases which are not too far advanced, suitable treatment if persevered with, may in time produce resolution and restore function.

In subacute and chronic gonococcal arthritis, wasting of muscles acting on the joint is a feature, the result of a specific myositis. It is even more pronounced than in a tuberculous arthritis.

DIAGNOSIS of ACUTE GONOCOCCAL ARTHRITIS.

Acute monarthritis or polyarthritis occurring during an attack of acute gonorrhoea offers no difficulties in diagnosis. The presence of the gonococcus can be demonstrated in the accompanying urethral, cervical or other discharge, and if necessary, the diagnosis can be completed by the isolation of the organism from the joint fluid. Joint puncture, however, is an unnecessary procedure in the majority of cases, and unless performed with strict asepsis may be responsible for the introduction of other pyogenic organisms into the joint, with resulting pyarthrosis. It has been pointed out that in the case of the aspirated joint fluid, negative cultural findings cannot be regarded as proof that the arthritis is not gonococcal in origin.

In patients presenting themselves for examination for the first time, a diagnosis is made by local examination of the affected joints, by careful inquiry into the history of recent exposures to, and by symptoms of gonococcal infection, and by a thorough examination of the genito-urinary tract, for signs, and bacteriological proof of the disease. A

denial/

denial of gonorrhoea is not always to be relied upon especially in the case of women, because they are often ignorant of its presence.

In women the urethra, para-urethral ducts, Bartholinian glands and ducts, the cervix uteri, uterus and uterine tubes, are examined systematically. Specimens of doubtful secretions obtainable from these parts are examined for the presence of the gonococcus, either by direct film or culture.. Film preparations should be stained by Jensen's modification of Gram's stain. By this method gonococci and other Gram-negative micro-organisms, stain red: Staphlococci and Streptococci and all other Gram positive micro-organisms stain black or purple.

In men a routine examination is made of the urinary meatus, openings of Tyson's gland ducts, urethra, Cowper's glands, prostate, seminal vesicles and epididymus. Valuable knowledge as to the condition of the urethra and the ducts and lacunae opening into it, is obtained by means of the two glass urine test, and by direct examination with the urethroscope. Urethral and prostatic smears are examined for the presence of gonococci. The latter are taken only after the acute infection in the prostate and vesi-

cles/

vesicles has subsided, and it is permissible to massage them, and after the urine in the second of the two glasses has become clear.

If direct films are repeatedly negative, cultural methods should be employed before excluding gonococcal infection. Cultures are made from the urethral discharge, and from the centrifuged deposit of urine voided subsequent to prostatic and vesicular massage. Every precaution should be taken to prevent the specimen of urine becoming contaminated with other organisms during its collection.

If negative bacteriological reports are obtained, in cases where gonococcal infection is suspected, it is essential to repeat the smears and cultures 24 to 48 hours after an intramuscular injection of a polyvalent vaccine, containing 300 to 500 million gonococci in the dose. This acts as a powerful provocative by stimulating focal infections to increased activity, after which one has a better opportunity of isolating the infecting organism.

The prostate and seminal vesicles should be palpated carefully, by digital, rectal examination, for pain, tenderness, and variations in size and consistency. The presence of certain symptoms such as urgency/

urgency of micturition, suprapubic pain, pain in the rectum, pain and bleeding towards the end of micturition, and painful erections, suggests involvement of these organs.

If one realises the importance of careful examination of the genito-urinary tract in all cases of acute arthritis, the error of overlooking a possible gonococcal infection as the underlying factor responsible for the joint condition, will not occur.

At its onset acute gonococcal arthritis may simulate acute rheumatic fever, but many points of difference soon become apparent. In the latter condition, arthritic symptons tend to be more acute, the temperature is higher, usually between 103° and 105° Fahr., more irregular with marked remissions and exacerbations, and prostration is much greater. Profuse perspiration is commoner and at first has an acid reaction and a peculiar sour odour. Sweating and chills at all comparable, are only a feature of gonococcal arthritis, when suppuration supervenes.

In gonococcal arthritis only one joint may be affected, an unusual feature in rheumatism, and

if/

if a number of joints become involved, symptoms invariably persist in the first joint affected; in acute rheumatism the pains exhibit a marked tendency to migrate from joint to joint, the earlier joints affected becoming symptom-free as the arthritis becomes more widespread.

Associated with acute gonococcal arthritis, there is usually a concomitant tenosynovitis and involvement of aponeuroses and fasciae.

Certain joints such as the mandibular, sternoclavicular, and sacro-iliac, not infrequently the seat of gonococcal arthritis, are practically never affected in acute rheumatism.

A history of previous attacks or of recurrent arthritis is suggestive of a diplococcal infection, and salicylates, so valuable in the treatment of acute rheumatic fever, have no effect on the pains or temperature in acute gonococcal arthritis.

COLLINS (34) (1921) states that he has administered as much as 120 grains of sodium salicylate in twenty four hours in the latter condition without relieving the arthritic pains.

The gonococcal complement-fixation test of the blood, which will be discussed later, is an additional/

additional aid to diagnosis and if positive, is diagnostic of a gonococcal infection. A negative test does not exclude the possibility of the arthritis being gonococcal. Taken early in the disease within nine or ten days of the first appearance of signs and symptoms of gonorrhoea, I have found the test invariably negative. In the two cases in which arthritic symptoms commenced five days after the onset of the urethritis, the test performed two days after the onset of the arthritis, was negative in each case.

X-Ray examination of the joints in acute cases is of little assistance in diagnosis. If the intra-articular effusion is marked, radiograms show a corresponding increase in the interval between the opposing articular surfaces, and there is usually slight haziness from swelling of the soft parts. Later absorption of cartilage results in narrowing of the cartilaginous space of the joint, and reduced density from atrophy of bone may be detected. None of these features are diagnostic of gonococcal arthritis; very similar radiographic changes are observed in the early stages of acute pyogenic arthritis. In the/

the latter changes in the cartilage and bone occur more rapidly, and are more extensive. Absorption of cartilage alone results in narrowing of the joint space, while absorption of both cartilage and bone produces obliteration of the space, and loss of the cortical shadow. In severe pyogenic cases the cartilaginous space may be entirely obliterated in one to two weeks from the onset, depending on the size of the joint.

Acute gonococcal arthritis must be differentiated from cases of multiple arthritis following acute tonsillitis, typhoid and scarlet fever, dysentery, cerebro-spinal meningitis etc. An accurate diagnosis can only be made after a careful and complete examination of the patient with a view to locating, and discovering the true nature of, foci of disease elsewhere in the body.

CHRONIC/

DIAGNOSIS of CHRONIC GONOCOCCAL ARTHRITIS.

So numerous are the causes of chronic arthritis, that it is one of the most difficult problems of medicine to establish an accurate diagnosis. In the majority of cases some underlying bacterial infection will be discovered; but other aetiological factors, such as faulty metabolism, endocrine dysfunction, trophic disturbance, and trauma are frequently responsible. SIR THOMAS HORDER (35) (1923), maintains that the microbic factor is invariably present, either alone or in association with other factors.

Chronic gonococcal arthritis belongs to that large group of chronic joint diseases due to a specific infection, and has to be diagnosed from other types in the same category; for example, arthritis produced by the tubercle bacillus, spirochaete pallida, streptococcus, pneumococcus, bacillus dysenteriae and the bacillus coli communis.

It must be differentiated also from chronic infective or 'rheumatoid' arthritis, osteo-arthritis, and climacteric arthritis, from chronic gout, and the arthropathies complicating tabes dorsalis, syrin-

go/

syringomyelia, hemiplegia, and paralysis agitans.

When investigating any case of chronic arthritis, the possibility of its being gonococcal in origin, should always be borne in mind.

A complete and thorough clinical examination of the patient is essential, and every available method of diagnosis should be utilised. A good history must be obtained by tactful inquiry, the chief points to be elicited being the possibility of existing gonorrhoea; of previous attacks - whether untreated, partially treated or cured; of arthritis complicating these attacks - its nature, duration and distribution. Valuable assistance in excluding other conditions liable to produce chronic joint disease, can be obtained by further questioning.

Urethral and prostate smears and cultures taken subsequent to the injection of a polyvalent gonococcal vaccine, are necessary to exclude a gonococcal aetiology. In women urethral and cervical smears and cultures are taken before and after a menstrual period, or if necessary after a provocative injection of vaccine. Clinical examination is directed especially towards the prostate and vesicles in the male, and to the cervix, uterine tubes, and Bartholinian glands, in the female, because these are the parts most likely to harbour latent gonococci, and

give/

give rise to metastatic involvement. X-Ray examination is of considerable help in differentiating between gonococcal and other forms of chronic arthritis, in revealing the extent of the cartilaginous and osseous changes, and in excluding a superadded 'rheumatoid' condition.

The diagnosis of gonococcal arthritis is often simplified by the discovery of concomitant metastatic and toxic lesions of gonorrhoea. In my series of 119 cases, there were signs and symptoms of recurrent iritis in one case, keratodermia blennorrhagica in another case, and exostosis of the os calcaneum in five cases.

Although gonococci have never been discovered in the eye, either by smear or culture, in cases of iritis occurring in conjunction with gonorrhoea, the majority of observers who have written on the subject are of the opinion that iritis is a true metastatic, and not a toxic lesion, the organisms being conveyed to the iris by the blood stream through the anterior ciliary arteries. If the true nature of this condition is unrecognised and the primary infection left untreated, recurrences are common. The presence of iritis, or a history of recurrent/

recurrent iritis in association with chronic arthritis, is a point in favour of the joint lesion being gonococcal in origin; and a history of acute gonorrhea occurring many years before should not oppose, but rather support this diagnosis because many instances of metastatic infection supervening at a very remote period after the original infection, have now been reported.

Keratodermia blenorrhagica, or gonorrheal hyperkeratosis, is definitely a lesion dependent on gonorrhoea, and is, therefore, of diagnostic importance when it occurs in cases of obscure arthritis. It is a rare condition, being present in only one of 3,000 consecutive cases of gonococcal infection in the male, and not occurring in any of 1,000 consecutive female cases, that I have studied. D. LEES (36) (1922), stated that only 47 cases had been reported in the literature. It is usually associated with severe gonococcal arthritis or polyarthritis, in patients whose general health has been undermined, and who are thin, anaemic, and wasted. It usually commences during the fourth or fifth week of the infection, as small talangiectatic spots or red vesicles, which later develop into papules with a horny centre and hard bases, and the lesions, at first discrete, tend to/

to coalesce. These cones are at first dull pink in colour, surrounded by a faint pink areola, but later become yellowish brown; skin lying between adjacent cones becomes thickened and assumes the same colour as coalescence takes place. The balls of the great toe, the margins of the sole and heel, and palmar surface of the hands, are the parts most commonly affected, and the lesions are markedly symmetrical. In severe cases the trunk, extremities, face, scalp, and genitals may be affected, and the nails may become enormously thickened and eventually slough off. After lasting for some weeks or months the crusts are cast off, leaving a reddened surface glazed by a thin epidermis. The gonococcus has not been isolated from these skin lesions, so it has been suggested (JEANSELME, 1895), that the condition is due to a gonococcal toxin acting either directly on the skin, or indirectly through the nervous system, producing trophic changes.

Exostoses, especially of the os calcaneum, are sometimes met with in association with gonococcal arthritis, and if present, are additional facts to substantiate a diagnosis of the latter condition; but their presence alone is not pathognomonic of an underlying gonococcal infection, as they not infrequently result from other causes.

The/

The common variety, characterised by pain on pressure over the plantar surface of the heel, is situated at the medial process of the tuber calcanei, just in front of the attachment of the plantar fascia, and its presence is revealed in a radiogram. The 'spur' appears of less density than normal bone and the distal extremity is somewhat larger than the portion attached to the bone; and variations in size from a pea to a marble are met with. In association with an Achillobursitis exostoses may be present on the posterior surface of the bone. In the five cases I have mentioned, the exostosis was at the usual site on the inferior surface, and the condition was bilateral in four of them. MERRIT (37) (1917) believes (and this is the view generally held) that the exostosis commences with proliferation of the osteogenic layer of the periosteum and later becomes ossified and firmly attached to the underlying bone. BAER (38) (1906) was of the opinion that the disease commenced in the flexor digitorum brevis muscle and extended down to the bone, and that the periosteum was not primarily, but secondarily involved. He removed the 'spur' in five cases by operation; in one he was able to isolate the gonococcus in culture, and in three others demonstrate the organism in/

in stained sections. JAEGER[39] (1908) reported on eleven cases and considered the process to be an ossifying periostitis; he also claimed to have succeeded in isolating the gonococcus in one of his cases. These positive findings have not been confirmed by other authorities, although it must be admitted that very little, so far, has been published on the subject.

GONOCOCCAL/

GONOCOCCAL COMPLEMENT-FIXATION TEST OF THE BLOOD.

The gonococcal complement-fixation test of the blood is of decided value in the diagnosis of acute and chronic gonococcal arthritis. A positive test is proof of present or recent gonorrhoea, whereas a negative reaction does not exclude this possibility. In my series of cases it was positive in 73.3% of chronic, and in 61.1% of acute cases. I have excluded seven cases in which the test was performed within nine days of the appearance of the first signs and symptoms of the urethritis, and was not repeated during the course, or after the occurrence of the joint complication. Taken so early in the disease it is invariably negative.

The greatest field of utility for the test is in those cases of suspected gonococcal arthritis, where repeated examination has failed to reveal the presence of the gonococcus. A positive result is strong evidence in support of a diagnosis of gonococcal arthritis. It may be accepted as a general rule that in cases with a negative reaction, combined with negative clinical and cultural findings in the prostate and seminal vesicles, it is safe to conclude that the arthritis is not gonococcal in origin.

In/

In a discussion on the value of the gonococcal fixation test in diagnosis, WILSON FORBES & SCHWARTZ,[40] (1923) conclude that "the negative tests that control human sera indicate that the gonococcal fixation test is specific", and that "it is an aid to the clinician in institutional work". Of their cases in the acute and subacute stages, 47% were positive, while in chronic cases 73 were positive. Of doubtful cases 60% were positive.

SIR THOMAS HORDER[41] (1923), reviewing these results remarkes, "Bearing in mind the fact that it is the chronic cases that we are denied the advantages of direct bacteriological proof, the smaller percentage of positive results in the acute and subacute cases is not such a material loss as might at first be thought".

BEZANÇON, WEIL, & RUBINSTEIN[42] (1925) performed the gonococcal fixation test in 24 undoubted cases of gonococcal arthritis with 21 positive results, a percentage of about 87.5. Fourteen patients suffering from non-gonococcal affection of the joints, all gave negative results. They remark upon its special value in the diagnosis of cases of obscure chronic arthritis.

THOMSON/

THOMSON[43] (1923) performed the test in twenty cases of acute gonococcal arthritis from one to thirty days duration and found it positive in every case (100%), and obtained positive results in 94% of thirty three chronic cases of one to twelve months duration, or longer.

Other varieties of arthritis always give a negative result, unless complicated by gonorrhoea. The test is, therefore, a most valuable aid in diagnosis.

TREATMENT

In reviewing the literature on gonococcal arthritis one is struck by the large number of entirely different methods of treatment that are in existence at the present day. Some authors report excellent results from treatment directed only to the local arthritic condition, there being no mention whatsoever of the importance of eradicating the primary infection at the same time, while others place such faith in focal treatment by special, usually operative methods, that local treatment of the affected joints, is considered unnecessary. Diverse opinions also exist as to the relative value of vaccines, sera, non-specific proteins, and chemotherapentic agents in aiding recovery in cases of gonococcal arthritis; the majority of workers favour specific immunization with gonococcal vaccines, while some believe that these are not specific and results just as good follow the use of other vaccines.

I quote THOMAS (44) (1927) who says, "Extensive observations and direct inquiries relative to the treatment of gonococcal arthritis, both by orthopædists and urologists, have revealed the greatest/

greatest disparity and pessimism, in the management of this often unwelcome and obstinate condition. The variability of treatment is striking and unquestionably accounts for many indifferent and poor results. I doubt whether there is any disease in the whole category of medicine where to-day more inconstant and conflicting opinions exist, relative to treatment".

It is of the utmost importance to appreciate fully the value of early treatment. If therapeutic measures known to be effective are adopted sufficiently early, the unfortunate occurrence of prolonged or permanent joint disability, which results so frequently from inadequate and faulty treatment, and inevitably follow lack of treatment, can be avoided. Most favourable and hopeful end-results are to be expected in cases revealing clinical signs and symptoms of a synovitis, where X-ray examination shows no signs of cartilaginous or osseous destruction or prolification.

It has been pointed out already that arthritis of gonococcal origin complicates disease alsewhere in the body and is never a primary condition. Hence the fatuity of attempting to obtain permanently/

permanently good results by local treatment alone. Until the primary source of the infection is eradicated, septicaemia, and consequently arthritis, is liable to recur.

There is no specific treatment of gonococcal arthritis. The best results are obtained by a combination of local, focal, and general measures.

LOCAL TREATMENT in ACUTE GONOCOCCAL ARTHRITIS.

Relief of pain and reduction of swelling are the first essentials of local treatment. Early immobilization of the affected joints, with the patient in bed, is most important. In the lower extremity this is achieved by the application of a suitably padded poroplastic splint, or in some cases sandbags to steady the limb, will suffice. In the upper extremity a sling, and a bandage enveloping the chest and upper arm in addition in severe shoulder cases, is all that is necessary.

Suitable soothing preparations are applied twice or three times during the day locally. Any of the following dressings may be employed: antiphlogistine, lead and opium, ichthyol 10 to 50 % in glycerine, glycerine of belladonnaa, or Methyl salicylate/

salicylate in equal parts of ol. olivae, WOLBARST (45) (1928) recommends the following ointment for local use

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Ichthyoli	1½ drachms.
guaiacoli	½ drachm.
pulv. opii	½ drachm.
lanolini ad	1 oz.

/n

Bier's method of passive hyperaemia is of immense value in relieving pain, and it is recommended from the beginning of the attack. The bandage should not be applied too tightly and congestion is maintained continuously for twenty hours, and then discontinued for a few hours, during which time the limb should be slightly elevated..

As the acute condition subsides, local applications of ung. hydrarg co. (Scott's dressing) or iodex are useful in stimulating absorption of inflammatory products. If the pain and swelling persist for sometime a moderate degree of counter-irritation of the skin over the joint is helpful, but preparations liable to injure the skin, such as the too frequent application of tinct. iodi, or blisters, should be avoided. Capsicum ointment containing 40 grains of salicylic acid in the ounce applied on lint twice/

twice daily, is an excellent preparation which will not blister the skin if removed at the end of twenty to thirty minutes.

Hot air baths are useful at all stages of the disease. They are continued for half and hour twice daily, at first, and later as the acute inflammation subsides the temperature can be raised, and the treatment maintained for an hour, all dressing being removed from the joints. These baths, by producing active hyperaemia, diminish joint pain, and favour absorption of inflammatory products.

Local electrical treatment in the form of continuous currents, or in the shape of ionisation with salicylates is frequently used by some, chiefly for the relief of pain, but the results obtained are no better than those following the use of Bier's congestion.

TREATMENT BY DIATHERMY.

In October 1913 diathermy was first used in the treatment of gonococcal arthritis by CUMBERBATCH (London). Since that date CUMBERBATCH and ROBINSON (46) have recorded results obtained in thirty nine cases.

The/

The local application of heat to a joint by means of hot fomentations or hot air, permits of the tissues below the surface being heated for a short distance only. This is due to the fact that the tissues conduct heat very slowly and the heat is rapidly dispersed by the circulation in the minute vessels, arterioles, capillaries and venules and possibly in the lymphatics. When the diathermy current, which is a "high frequency" alternating electric current, is passed through the body the tissues become heated en masse; the passage is so rapid that loss of heat by convection plays a negligible part. Diathermy has the advantage over continuous electrical currents in that it produces heat without causing any chemical (electrolytic) changes in the tissues, or stimulation of nerve or muscle.

It is a well known fact that the lethal temperature for the gonococcus is relatively low. According to SANTOS (47) (Lisbon) gonococci are killed in culture by an exposure of 133°Fah. for 37 minutes, and by an exposure of 109°Fah. for 76 minutes. Jordan in his text book of "Bacteriology" states that cultures are injuriously affected by a temperature of 104° to 105°Fah. In MacFarlane's "Pathology" it is/

is stated that the gonococcus is injured or destroyed between 102·2° and 104°Fah.

In the tissues, as in cultures, a rise of temperature is prejudicial to the existence of the gonococcus. This is revealed by the rapid disappearance of the organism during pyrexial attacks, brought about by the incidence of malaria, during the course of a gonorrhœal infection, as in cases reported by CULVER (48) (1917) and others, or by the injection of a foreign protein.

In diathermy we have an ideal means of producing local pyrexia which will have a deleterious effect on the gonococcus. Besides this direct effect on the organism, CUMBERBATCH and ROBINSON maintain that because cell metabolism is stimulated, tissue resistance to infection is increased; there is an increased blood supply to the part which favours the absorption of exudates, and antitoxin formation is stimulated.

Of the thirty nine cases of gonococcal arthritis, including acute and chronic varieties, that they record, all, with the exception of two in which treatment could not be completed, derived the greatest benefit from diathermy. At first treatment was restricted to local exposures to the joints, but later/

later, better results were obtained by combining this with similar treatment directed to the primary focus in the prostate, seminal vesicles, and urethra in the male, and in the urethra, cervix, and uterine adnexa in the female. In acute and subacute cases, the symptoms disappeared and the joints were soon restored to full functional activity. In chronic cases pain was abolished, swelling subsided, and the range of movement increased. They conclude that "if the dire results of long-continued arthritis be remembered, it may be claimed that the results of treatment by diathermy are far superior to those obtained by any other method".

These authors advise treatment of the joints and primary foci twice or three times a week. Three to five applications of diathermy are usually sufficient for eradicating disease of the female urethra and cervix uteri, each part being treated for ten minutes. Seven to eight applications to the prostate, posterior urethra and seminal vesicles (treated simultaneously for twenty minutes) are usually sufficient. The number of applications to the joints varies in different cases. In some, treatment of the original foci alone, causes the joint pains to subside; in other cases eight to twelve applications/

applications to the joints are necessary.

As soon as the acute symptoms have subsided, immobilisation is discontinued and massage is commenced. Massage is an excellent additional therapeutic measure; it is soothing, favours absorption of inflammatory exudates, diminishes swelling, and is beneficial in toning up the muscles acting on the joint. At first it is performed very gently twice daily and combined with slight passive movements of the affected joint. Massage and passive movements are gradually increased and the patient later is encouraged to carry out active movements. By the institution of early massage and movement the risk of subsequent disability from adhesions is avoided.

COLLINS (40) 1921 advocates more complete and longer immobilisation in all acute gonococcal joints. The plan he adopts at the Bellevue Hospital, New York, is to encase the affected joints in Plaster of Paris, including the joints above and below as well. This case is removed after two weeks to permit of massage and passive movement. Then the skin is rubbed with alcohol, and the plaster reapplied for two weeks. At the end of this time immobilization is stopped and massage and movement recommenced/

recommenced. Radiant heat by hot air baths is applied to the affected joints for 30 minutes, the temperature being 150°F. From the fourth to the seventh day the temperature is raised to 200°F. for one hour daily. After a week more active massage is given. Ten days after the final removal of the cast the patient is able to commence walking, beginning at first by pushing a chair slowly around the room. COLLINS states that this method of treatment is efficient in preventing such complications as ankylosis and suppuration, and from the moment of application the patient is completely freed from pain. He quotes one case in which the spine, hips, knees, and ankles were acutely affected. Even the slightest movement caused the patient to cry out in pain. A plaster case stretching from axillae to toes was applied for a month. Thereafter physical therapy was adopted. When the patient was discharged at the end of seven weeks, he was walking well with good functional results in all the involved joints.

COLLINS' method of immobilization will certainly eliminate the pain of an acute joint; but it is difficult to visualize how subsequent ankylosis is to be prevented, when one realises how great is the/

the risk of ankylosis, because of the sero fibrinous exudate in acute gonococcal arthritis, and that encasement in plaster will render early massage and movement impossible. His method is not to be recommended.

JOINT PUNCTURE and ARTHROTOMY.

If there is much distension of the joint accompanying the acute arthritis, HARRISON (50) (1920) recommends aspiration of the joint contents as a valuable means of relieving pain, and assisting recovery. A stout needle is used and every precaution taken to procure strict asepsis. MURPHY (51) combines aspiration with the introduction of 5 to 15 c.c. of a 2 % solution of formalin in glycerine into the joint. Joint puncture is not to be regarded as a routine method of treatment in all cases of acute gonococcal arthritis exhibiting distension. In the majority of cases, intra-articular effusion readily subsides with other local measures previously mentioned. Joint puncture was not found necessary in any of the acute cases I have studied.

CHURCHMAN (52) (Yale University) published in 1918 and 1920, results obtained by joint puncture followed/

followed by intra-articular medication with gentian violet, in a series of cases of acute infective arthritis, including eight cases of gonococcal arthritis of the knee. A large needle is inserted into the affected joint with aseptic technique. Then with the aid of a special apparatus which he has designed, and which he describes in detail, the joint fluid is aspirated, and 3% procain or novocain solution is introduced. By adjusting the necessary taps of the apparatus, the joint is flushed in turn with saline solution, hydrogen peroxide, and then with saline solution again. In this way mucus, fibrin and pus, are dislodged and removed from the interior of the joint. A solution of 1:1000 gentian violet is then run in and allowed to act for five minutes. After this solution has been aspirated, and before the needle is withdrawn, a solution of 1:10,000 gentian violet is introduced and left in the joint. If necessary the procedure may be repeated in a few days.

He assumes that organisms lying on the synovial membrane or loose in the joint are killed by the stronger solution, and if they escape, their development must be retarded by the presence of the weaker solution in the joint. In support of this theory/

theory, CHURCHMAN has demonstrated experimentally, that gentian violet kills Gram-positive organisms with great ease, prevents the growth of Gram-negative organisms in strong solution, and if applied to a mucous surface, it reaches its depths. That it has no deleterious effect on the synovial membrane is borne out by the complete lack of reaction following its introduction into the joint.

He reports excellent results in cases of acute non-gonococcal arthritis. With regard to the eight gonococcal cases he states in his summary that, "making due allowance for the mild character of the cases treated, (they were not selected ones) and for the fact that complete bacteriological proof of cure could not always be obtained, a satisfactory clinical course warrants the belief, that lavage and staining offer a method of controlling the disease. Such bacteriological evidence as it has been possible to obtain, strengthens this conviction."

WALTHER[53] (1914) and MOBITZ[54] (1920), also favour joint puncture followed by antiseptic lavage in cases of acute gonococcal arthritis. PLISSON[55] (1927), recommends opening the joint either by puncture or large incision. After washing out the cavity completely, he introduces anti-gonococcal/

gonococcal serum 10 to 20% in physiological saline, into the joint. In his experience this method, combined with early and thorough treatment of the primary infection gives the best results.

In a discussion on the treatment of gonococcal arthritis FREIBERG (56), Cincinnati, (1927) states that when the synovial membrane is the chief seat of the infection, and there is an effusion, the most rational measure, and a method which has given very satisfactory results in his hands, is to open the joint through a small incision, and flush it freely with hot water at a temperature of 115°F., which the body will easily bear. In this way the gonococcus, which he states is killed at a temperature of 110° F., succumbs, all gelatinous and fibrinous deposit in the joint is removed, and resolution in the synovial membrane is stimulated by the active hyperaemia produced. When the joint has been sufficiently irrigated, the incision is closed without drainage.

In 1899 JOHN O'CONOR (57), reported good results in ten cases of gonococcal arthritis with effusion, which he treated by arthrotomy, followed by joint irrigation, and drainage. The knee was affected in eight cases, including one bilateral, and one/

one wrist case. The ankle was affected alone in one case, and a wrist joint in another case. With the exception of one case which was then under treatment, complete function was restored in all. The drains introduced at operation were removed on the third day. In no case did sepsis supervene and no relapses occurred. So impressed was he with this method of treatment, that he strongly recommended other surgeons to practice early arthrotomy and "save the joint structures from prolonged immersion in a particularly destructive exudate".

KLOSE (58) 1919 basing his conclusions on experience at the University Hospital, Frankfort-on-Main, since 1909, strongly advocates arthrotomy in selected cases of severe gonococcal arthritis. He maintains that arthrotomy should be performed in cases when renewed effusion, with considerable distension of the joint capsule and with pain, follows aspiration; when signs of sublaxation are becoming evident; when the inflammation is phlegmonous, and pain and sleeplessness are alarming; when severe complications interfere with conservative treatment; when many joints are involved and their simultaneous treatment is not feasible, and when three weeks of skilled conservative/

conservative treatment has failed. Pain is instantly relieved by the operation and the condition begins to improve at once. With the exception of 14% of his cases, where the disease had already progressed so far that ankylosis was unavoidable, he obtained good functional results.

None of the cases of acute gonococcal arthritis I have seen have been treated by arthrotomy and joint lavage. Judging of the cases recorded by those who advocate arthrotomy, good results consistently seem to follow the operation, but equally good and usually better results can be obtained much more easily with conservative measures, without running the ever present risk of transforming a simple synovitis into a pyarthrosis, by the introduction of other micro-organisms. I believe that arthrotomy is an unnecessary procedure in the average case of gonococcal arthritis, its only indication being in cases where suppuration has occurred. In these cases of purulent arthritis it is essential. Under general anaesthesia the joint cavity is freely opened, and washed out with some suitable antiseptic such as eusol. Thereafter irrigation and drainage are maintained until the condition subsides.

CHRONIC/

CHRONIC GONOCOCCAL ARTHRITIS.

LOCAL TREATMENT.

BIER'S congestion is valuable in relieving pain, which is never as severe as in acute gonoccal arthritis. It also promotes resolution. When the bandage is not in use, active hyperaemia is instituted by radiant heat, diathermy, or counter-irritation by stimulating applications, such as iodex and methyl salicylate ointment, or one of capsisum and salicylic acid. The latter preparation is applied in the same strength as in acute cases and is not rubbed in; it is allowed to act for half an hour. Iodex should be well massaged into the skin. In addition, the affected limbs are massaged twice a day, to hasten absorption of inflammatory exudation, and to maintain and increase the tone of the muscles acting on the joint. Massage is combined with gradually increasing passive and active movements, until full functional activity is re-established.

In cases of hydrops articuli in which the effusion is moderate in amount, the best results are obtained/

obtained by applying Scott's dressing (ung.hydrarg. co.) to the affected joint, the lint is covered with wool and an elastic bandage applied to exert firm and uniform pressure; this dressing may be retained for about three days before renewing it. If the effusion is marked and does not respond to this treatment, it is advisable to aspirate the joint and relieve the intra-articular tension.

If adhesions are present, and stiffness and limitation of movement persist in spite of massage and other local treatment, a general anaesthetic is required to enable one to mobilize the joint by breaking down adhesions. Before performing mobilization under anaesthesia, it is essential to X-Ray the joint. This is especially important in old standing knee cases, where firm bony ankylosis may exist between the patella and anterior surface of the lower end of the femur. If the joint is forcibly flexed, the infra-patellar ligament will rupture or be severed from its attachments.

When the disease has progressed beyond the stage where success could be expected to follow conservative treatment, where advanced degeneration and proliferative/

proliferative changes exist, operative treatment by arthroplasty or arthrodesis, holds out the best hope of relief from this disabling and crippling condition.

FOCAL TREATMENT.

In all cases local treatment of the affected joints should be combined with treatment directed against the focus, or source of infection. Neglect of this is responsible for many failures and poor results. In the presence of re-innoculation of the blood-stream, with organisms derived from an uncured focus of infection in the genito-urinary tract, and consequently reinfection of the joints, local measures alone invariably fail to establish a permanent cure; acutely infected joints pass into a chronic state of infection with resulting structural changes, acute exacerbations are prone to re-occur in chronic joints, and joints in which resolution has followed appropriate local treatment, are liable to recurrence of the infection.

FOCAL TREATMENT IN MEN.

If the joint symptoms are very acute, any treatment that necessitates moving the patient is contra-indicated/

contra-indicated. The anterior urethra is gently irrigated twice or three times a day, and a rectal suppository containing morphine gr ¼, or one containing antifebrine grs.iv. and atropine sulphate gr.1/75, is given to diminish the severity of the acute prostatitis and vesiculitis; the former will only be required during the first few days.

Later when the patient can be moved, irrigation of the posterior urethra, hot rectal douches, and antiseptic hot hip baths are commenced and repeated twice or thrice daily. When gonococci are abundant in the urethral smear, the most satisfactory solutions for use as irrigations, are:- 1:8000 permanganate of potash, 1:4000 mercurochrome 220, or 1:6000 albargin. Later if other pyogenic organisms are found, solutions of 1:5000 chloramine T., 1:5000 oxycyanide of mercury, or 1:20,000 perchloride of mercury are more serviceable, and in the resolving stages of the urethritis astringent lotions such as 1:2000 "nizin" (zinc sulphanilate), 1:1000 sulphocarbonate of zinc, or 1:6000 permanganate of zinc are preferable. Initially the temperature of the irrigating fluid should be 104° to 106° F., but as the condition subsides, the temperature is raised to/

to 108 to 110° F. For anterior irrigation the irrigation can should be at a height of 2½ ft. above the patient's pelvis; for posterior irrigation the height should be from 3 to 4 ft.

When the acute prostatic and vesicular symptoms have subsided, rectal douches may be discontinued, and the antifebrine-atropine suppository replaced by one containing ichthyol grs.V. and atropine sulphate grs.1/75. The ichthyol promotes resolution of the inflamed prostate and peri-vesicular tissues.

Prostatic and vesicular massage may be commenced after the urine, as demonstrated by the two glass test, has been clear for three or four days. Massage is one of the most important therapeutic measures we possess for the eradication of infection in the prostate and vesicles; retained inflammatory exudates in the vesicles and in the alveoli of the prostatic gland, are expressed into the posterior urethra; the circulation of blood in these organs is augmented, and it is highly probable that after massage a certain amount of the expressed inflammatory débris, rich in organisms, is absorbed, and in virtue of its antigenic properties, stimulates the formation of specific anti-substances in the blood.

At first the massage must be gentle; later more active massage is instituted and repeated bi-weekly until the prostate and vesicles have regained their normal size, contour, and consistence, and until prostatic smears contain no pus cells or gonococci, and sperm cultures are sterile.

In cases with chronic prostatitis and vesiculitis, massage must be employed similarly, twice weekly. As a rule in these cases, urethral and prostatic smears reveal the presence of other micro-organisms, in association with the diplococcus of Neisser, and the urethral discharge is slight. In other cases, although the history and clinical findings suggest an uncured gonococcal infection, it may be impossible to demonstrate the gonococcus; a chronic gleet is present, most noticeable in the mornings, the urine in both glasses is slightly hazy, the second containing comma-shaped threads characteristic of a prostate origin, and irregularities of contour, enlargement, and probably, tenderness of the prostate and seminal vesicles are demonstrable by rectal examination. In these cases the entire urethra should be irrigated on alternate days, or bi-weekly, with 1:5000 chloramine T., or oxycyanide of/mercury

of mercury. It is important to wash out the urethra subsequent to prostatic massage, the temperature of the solution being from 108 to 112° F. The massage establishes drainage from the prostatic ducts, and the subsequent irrigation clears away their expressed contents, destroys the infecting organisms, and increases the blood supply to the posterior urethra. In chronic infections of the prostate, the passage of a curved sound of fairly large calibre, size 24 to 26 (French Scale), assists in opening up the prostate ducts, and in promoting drainage from them. The instrumentation should be carried out in the intervals between the massage.

If the prostatic infection resists treatment by massage and subsequent lavage, success frequently follows the instillation of a solution of 1 to 2% silver nitrate into the posterior urethra, by means of an Ultzmann's syringe. A few cc. of the solution are instilled after prostatic massage. If frequency or urgency of micturition follows treatment by this method, mercurochrome 1% may be used instead of the silver solution, or suction of the prostatic ducts by the posterior suction apparatus of Mills, may be performed as an alternative.

After a course of massage of six to eight weeks/

weeks duration, it is advisable to rest the patient from this treatment for two or three weeks before recommencing. In the majority of cases a second course is unnecessary.

In cases of occlusion of the ejaculatory ducts, in which drainage from the vesicles is not re-established by the passage of a posterior sound of the Beniqué or Guyon type, followed by vesicular massage and without lavage, or by the instillation into the posterior urethra of silver nitrate in 1 to 2% solution, the ducts should be catheterised and irrigated. This somewhat difficult and delicate operation is performed with the aid of posterior urethroscopy. A fine Geraghty syringe with a blunt pointed needle is passed along the lumen of the posterior urethroscope into the orifice of the ejaculatory duct. The ducts in turn are irrigated with silver nitrate solution.

VASOTOMY/

VASOTOMY and VASOPUNCTURE.

Sterilisation of infected seminal vesicles by means of antiseptic medication via the vasa deferentia, is claimed by those who practise it to be a most valuable method of treatment in acute and chronic gonococcal arthritis in men, who have also seminal vesiculitis.

Vasotomy and vesicular lavage was first introduced by BELFIELD (59) (1905). Since that date he has made numerous contributions to the literature on the subject. He has carefully studied the physiology and pathology of the seminal vesicles, and draws attention to several important facts upon which he bases his treatment. From his results the operation seems to be fully justified in certain cases.

The vas and vesicles usually accommodate 4 to 6 c.c. of fluid. If more than this amount is introduced the increased intra-vesicular pressure causes the sphincter muscle at the mouth of the ejaculatory duct to relax, and a portion of the fluid is expelled into the deep urethra. Xray screen examination of the vesicles filled with a solution of collargol reveals the presence of peristalsis, and

by/

by direct vision through the posterior urethroscope emission of the fluid from the ducts can be watched.

Being a viscus (like the stomach) enclosed in unstriped muscle, the vesicle automatically churns its contents, thus bringing the antiseptic solution, introduced into it, into touch with the infective agents. The antiseptic remains in the vesicle for a considerable time maintaining its germicidal action, and for several days, sometimes for weeks, the urine voided may be stained black or brown by the retained silver solution, and seminal emissions are likewise dark in colour.

BELFIELD states that a seminal vesicle, being a simple sac lined only by a few layers of columnar epithelium, entirely devoid of lacunae, follicles, or glands, is admirably suited for local treatment, even more so than the anterior urethra. Thus the fluid filling its lumen is brought into direct contact with the entire lining membrane.

In 1920 BELFIELD published details of his modified operative technique. Briefly the operation is performed as follows:-

After antiseptic cleansing of the skin of the groin, local anaesthesia is carefully infiltrated into the skin/

skin and underlying tissues between the superficial inguinal ring and the upper pole of the epididymus. The vas is isolated by palpation and fixed against the skin with two pairs of Braum's tenaculum lock forceps inserted at a half-inch interval. Their points pierce the skin and encircle the vas. By holding them apart an assistant puts the skin and underlying vas on the stretch. A support is placed behind the scrotum at this point, and an incision half an inch in length is carried down to the vas wall, which is incised. A strand of silk-worm gut is passed into the lumen and advanced for 8 to 10 inches to make certain the vas is patent. A blunt hypodermic needle or a fine silver cannula is threaded over the gut into the vas and the thread is withdrawn. A syringe is attached, and 10 c.c. of 1: 25,000 Methylene blue solution are slowly introduced to estimate further the patency of the seminal duct. Shortly after the vesicle is filled the patient has a desire to micturate and the voided urine, if no obstruction is present should show the dye. (BELFIELD states that in his cases the vas has been occluded in more than 1%) If the operation is performed immediately afterwards on the opposite side, this/

this test is carried out with a solution of dilute fuchsin.

If there is no obstruction, 20 c.c. of 5% collargol solution are slowly injected into the vas. This is followed in two minutes by 1 c.c. of sterile water to minimize the possibility of regurgitation of collargol, which although harmless to the mucous membrane, is capable of producing irritation in other tissues.

A silk-worm gut strand is threaded on a fine needle and passed proximally into the lumen of the vas for a distance of half an inch and then through the skin. The ends are knotted loosely. This thread serves as a drain and a guide for the re-introduction of the needle into the vas for subsequent injections. It should never be retained for more than five days.

The modified operation advocated by FRANK KIDD (60) (1923) differs in minor details from that of BELFIELD. He does not use the steadying forceps but separates the vas completely from the underlying tissues, and when injecting, obtains counter-pressure by pulling on a piece of sterile tape passed under the vas, and distal to the needle. He/

He introduces a few c.c. of warm saline, in place of the dyes suggested by BELFIELD, patency of the vas being assured if the fluid runs freely into the lumen. After the instillation of colloidal silver he leaves the cannula (Size 19 to 23) in situ, and draws the edges of the wound together by a mattress suture passed under the vas. When this is tied the vas is slung up on a bed of connective tussue securely anchored to the base of the skin. The cannula is attached to the skin by a fine silk-worm gut stitch passed through its two rings.

KIDD is of the opinion that success does not always follow a single instillation, and advocates at least three irrigations during the course of a week to effect unfailing cures. For subsequent medication the stilette is withdrawn from the aannula, a few c.c. of sterile water are injected, and if the fluid runs freely, 10 c.c. of 5% colloidal silver (CROOKES) are introduced. When removing the cannula the silk-worm gut mattress stitch is withdrawn, and the wound is manipulated by the fingers so as to loosen adhesions around the vas, and allow it to drop back into its proper place in the scrotum. If this very important point is/

is neglected, the vas may remain adherent to the skin and the opening may persist as a spermatic fistula.

Cases are on record, of occlusion of the vas following regurgitation of collargol and argyrol at the point of infection in the scrotum. They are, however, rare. Chlorazene Solution 1:200 is preferred by some (WOLBARST)[61]; it is said to be as efficacious as the silver preparations and this complication has not followed its use.

Recently BELFIELD and ROLNICK[62] have recommended the use of aristol, 10 grams stirred up in 30 c.c. of cod-liver oil, or goose oil. They state that these animal oils are absorbed more readily than the chemical solutions hitherto used, and because of this, the danger of injury to the vas and adjacent tissue is considerably diminished.

If occlusion of the vas should follow vasotomy a simple re-constructive operation is all that is necessary, the affected portion being excised and the cut ends united by a fine catgut stitch. (MAYO;[63] LYDSTON[64].)

Its advocates advise the operation, in acute, as well as subacute, and chronic cases. KIDD states/

states that in seven cases of obstinate and crippling arthritis in which he practised vasotomy and lavage, all were cured in three weeks, and, "their joint troubles simply melted away". In future he proposes to perform the operation in acute cases of gonococcal arthritis and vesiculitis. BELFIELD has reported no fewer than 83 cases of acute posterior urethritis, with acute vesiculitis and arthritis, where immediate amelioration has been obtained by vasotomy.

Referring to vasotomy in the treatment of cases of gonococcal arthritis, in which there is disease of the seminal vesicles, WOLBARST (65) 1928 says, "I have found it of the greatest value and regard it as the most dependable single measure for the relief of the condition. The joint lesion responds almost immediately to the attack on the focal point in the vesicles. Aided by the administration of diathermy and a polyvalent mixed vaccine I have seen a quick and lasting response in joint cases which have resisted all other treatment".

THOMAS (66) (Philadelphia)(1917) strongly advocated VASOPUNCTURE, in preference to vasotomy, claiming that subsequent narrowing at the site of injection is/

is less apt to occur. In this operation after the usual exposure, the vas is punctured with a fine hypodermic needle attached to a syringe, no incision being made into the vas wall. He uses 5% collargol for injection into the vas, but draws attention to a new prepartion of silver proteose (20%), a product of the Hare Chemical Laboratory of the University of Pennsylvania. It contains 40% metallic silver, is quite penetrating, non-irritating to the mucous membrane even in 70% strength, and compared with collargol, is comparatively inexpensive. After the injection the wound is closed. This operation designed for a single lavage of the vesicle is insufficient in the majority of cases, because, according to KIDD, at least three irrigations are necessary for a permanent cure.

VESICULOTOMY/

VESICULOTOMY and VESICULECTOMY

Radical operations for drainage or excision of diseased seminal vesicles, first introduced by FULLER in 1901, are seldom if ever necessary, and should never be performed until other therapeutic measures have failed. The results of these operations have not generally justified early expectations. Sterility without impotence follows vesiculectomy and not infrequently follows vesiculotomy.

Vesiculectomy is recommended by THOMAS (67) 1917 in cases of extensive peri-vesiculitis, especially if fibroid induration of the base and neck of the bladder with vesicular obstruction and retention of urine, is present. Vesiculotomy, according to the same author, is the procedure of choice in cases where the vesicles are essentially lobulated abscesses, provided all the collections of pus can be incised. He states that the operation is not always curative, because of the anatomical difficulty of draining every focal abscess, especially if incision is made in the dark, or by sense of touch.

MICHEL (68) (1919), has not been impressed with/

with the post-operative results of seminal vesiculotomy. His results do not compare favourably with those obtained by conservative non-operative measures.

CUNNINGHAM (69) (1921) and GREENBERG (70) (1927) report good results from the operation of vesiculectomy in resistant cases. CUNNINGHAM writes that there is no operation performed for a chronic condition with which he is familiar, that gives more striking results. With removal of foci, pain disappears from the joints often at the time of ether recovery, and large swollen joints have become normal in appearance, or nearly so, within 24 to 48 hours of the operation. Periarticular swellings, in his opinion, disappear more rapidly than those that are intra-articular, and a considerable period of time, and appropriate accessary treatment, are necessary to repair such defects as destruction of cartilage and changes in bone.

PREGL'S SOLUTION.

STELLWAGON and McCAHEY (71) (1927) report successful results in fourteen cases of gonococcal arthritis and vesiculitis, treated by the injection of Pregl's solution directly into the seminal vesicles through the rectum. The solution is an aqueous isotonic iodide and iodate one, containing 3% of available iodine. After cleansing the lower bowel with a copious enema, followed by rectal lavage with four quarts of boric acid solution, the patient is placed in the knee-chest position, and, with a syringe fitted with a long rigid needle, not more than 3 c.c. of Pregl's solution are injected into the vesicle. The needle should not be inserted too deeply or too high up. Owing to the osmotic properties possessed by this solution the fluid quickly diffuses throughout the tissues of the vesicles, and its therapeutic effect is carried to a point beyond the immediate area injected. No pain, reaction, or abscess formation, followed the injection. In all cases only three or four injections were necessary to cure the arthritis and eradicate the infection in the vesicles. These authors/

authors state that injections are especially indicated in cases of acute gonococcal arthritis, which are dependent upon acutely inflamed seminal vesicles.

FOCAL TREATMENT in WOMEN.

In acute gonococcal urethritis the same antiseptics are used for irrigation as in the male, but the solutions are stronger. The urethra is irrigated with permanganate of potassium 1:6000 after the external parts have been cleansed with eusol, and antiseptic hot hip baths, are taken twice daily. After a week or ten days the irrigating solution is changed to albargin 1:4000, or if mixed infection is present to chloramine T, 1:3000. As the condition subsides irrigations are given once daily, or on alternate days.

If threads are still present in the urine when it has become clear, a straight bougie should be passed, and the urethra massaged on it through the anterior vaginal wall. In this way the formation of submucous infiltrations is prevented, and good drainage is established from the ducts and lacunae.

Mills suction bougie may be used as an alternative.

In the resolving stages astringent zinc preparations such as nizin 1:1000, and zinc sulphocarbonate 1:1000 are used for irrigation. During menstruation all active treatment is avoided.

The condition clears up in from three to six weeks but before pronouncing a cure urethral smears, taken before and after three menstrual periods, succeeding apparent clinical cure, should be free from gonococci. During this period the mucous membrane of the urethra is examined with the urethroscope to exclude any chronic infection of the gland ducts, Skene's ducts, or the submucous tissue.

ACUTE INFECTION OF THE CERVIX UTERI.

If the joint condition permits of it, the patient should be kept in the semi - Fowler position to assist drainage from the cervix, and hot hip baths are commenced as soon as possible, and continued twice daily. Treatment of the cervix is begun whenever it is permissible to place the patient in the lithotomy position. In this position the external genitals are cleansed with eusol, and a bivalve speculum/

speculum, suitably lubricated, introduced into the vagina. The mucosa of the vagina and vaginal surface of the cervix, is swabbed with gauze soaked in eusol and then dried. A dressed Playfair's probe, saturated with either 1% picric acid in glycerine or aqueous solution, 10 to 20% mercurochrome, ½% acriflavine, 50% formaldehyde in glycerine, 10% lunosol or 10% neoprotosil, is passed into the endo-cervix, and the mucous membrane is covered with antiseptic as far as the internal os. Erosions of the external os are similarly treated, and then the cervical and vaginal surfaces are dusted with compound dermatol powder by means of an insufflator, and the speculum removed. In some cases it is advisable to leave a small strand of gauze impregnated with antiseptic in the cervical canal for ten or twelve hours. This treatment is applied twice daily at first; once a day or on alternate days, as the condition subsides. Direct applications to the cervix are more useful than vaginal douching which is not to be recommended. During menstruation when there is a liability to upward spread of the infection to the endometrium, liquor sedans ½ to 1 drachm should be prescribed with tincture of belladonna 5 to 10 minims thrice daily. It/

It is helpful also in diminishing the pain and severity of the period.

Treatment is carried out on similar lines in subacute and chronic cases, but less frequently. In cases with cervical erosion suitable applications are 2% solution of picric acid in rectified spirit, or iodised phenol. In resistant cases suction of the endocervix with Mill's cervical suction bougie is useful in removing plugs of débris from the openings of the racemose gland ducts and establishing drainage. It is more efficacious than either dilatation or curettage of the cervical canal. These procedures are contra-indicated in that they tend to spread the infection and set up a pelvic cellulitis.

ACUTE INFECTION OF THE UTERINE TUBES.

While acute symptons are present douching and other intra-vaginal treatment must be suspended. The Fowler position is maintained, and hot fomentations, or an ice bag, applied to the lower abdomen for relief of pain. The majority of pure gonococcal infections of the uterine tubes do well without operation, but if there is associated infection with streptococci/

streptococci, and other pyogenic organisms, operative interference will be necessary. Hence the importance of carefully watching the patient's response to conservative treatment. If abdominal pain and vomiting persist, if the temperature falls rapidly while the pulse rate continues to increase, and if there is muscular rigidity, it may be necessary to open the abdomen. If operation is required for the removal of a localised pus sac, or thought necessary on account of adhesions, better results will be obtained if it is performed when the condition is quiescent.

As soon as the hyperacute condition has subsided, hot vaginal douches at a temperature of 110° to 112°F., given gently, are commenced. If there is no exacerbation of the infection after two days, 20% ichthyol and glycerine tampons are inserted into the fornices after vaginal douching, and left in position for twelve hours at a time. As the condition improves, the interval between douching is lengthened and the tampons left in for thirty-six hours. Tincture of belladonna, seven minims, is given by mouth to allay spasm, and liquor sedans prescribed at the onset of menstruation. Tonics

are/

are valuable in the convalescence. LEES[72] (1927) advises the following mixture which has a combined tonic and aperient action.

R/

	Mag. sulph.	1½ ozs.
	Quin. sulph.	8 grains.
	Liq. strych. hydrochlor.	64 grains.
	Tinct. ferri perchlor.	2 drachms.
	Glycerini	2 ozs.
Sig. 3	Ag. menth pip	8 ozs.

To be taken three times daily after food. If pelvic adhesions are a marked feature; hydrarg. iod: rub, gr. 1/16th T.I.D. in pill is advised by the same author.

CHRONIC INFECTION OF THE UTERINE TUBES.

If the infection does not subside with treatment by hot hip baths, hot vaginal douches, and glycerine and ichthyol tampons, combined with vaccine or protein therapy, removal of the tubes by operation is necessary. As a rule the tubes are grossly diseased, and functionally useless.

BARTHOLINIAN INFECTION.

When acute and chronic gonococcal infections/

infections of the Bartholinian glands and ducts give rise to metastatic arthritis, the most satisfactory means of eradicating the infection is by complete excision preferably under general anaesthesia.

After the parts have been shaved and cleansed, an incision is made on the inner surface of the labium majus over the gland, & the skin is reflected backwards. The ideal procedure is to shell out the gland, with its capsule & duct completely by blunt dissection, care being exercised to avoid opening into the vagina. If this is possible the connective tissue cavity remaining is swabbed with weak tincture of iodine, its walls approximated with catgut, & the wound closed without drainage. If, in cases of Bartholinian abscess the capsule has ruptured and the surrounding tissue has become infected, the latter after excision of the disorganised gland and its capsule, is scraped thoroughly with a sharp spoon, and swabbed with tincture of iodine, or 1% spirit= solution of picric acid. Under these circumstances, and especially if it is thought that small portions of the capsule still remain, the edges of the wound are loosely approximated and a small piece of rubber dam/

dam is left in its lower end, to ensure drainage, and to promote tissue granulation in the deeper parts. After operation in acute cases, the patient should receive antiseptic hot hip baths twice or thrice daily, and antiseptic dressings to the labial surfaces.

Excision of the gland and its duct is often more difficult in chronic cases in which the gland is usually a fibrous mass. In all chronic cases it is important to scrape and cauterise at the completion of the dissection and to drain the wound.

In cases without suppuration, the drain should be removed at the end of twenty-four hours, otherwise drainage is maintained for at least three days, the rubber drain being removed each day for antiseptic cleansing and then replaced.

GONOCOCCAL CONJUNCTIVITIS AND VULVO-VAGINITIS.

In those somewhat rare cases in which arthritis follows gonococcal conjunctivitis and vulvo-vaginitis, skilled focal treatment is also of the utmost importance. If both conjunctivae are infected simultaneous treatment of both eyes is indicated; of the/

the condition is unilateral, the unaffected eye should be carefully guarded by a Buller's Shield and receive appropriate prophylactic therapy.

In cases of ACUTE gonococcal conjunctivitis drainage from the conjunctival sac is hampered by spasm of the lids behind which pus tends to accumulate. To obviate this it is essential in the early stages to wash the adjacent ocular and palpebral surfaces, every half hour with a warm solution of saline or weak boracic acid containing five grains of sodium bicarbonate to the ounce, the solution being applied by means of a glass undine; If this is neglected there is considerable risk of corneal ulceration. A few drops of a silver solution, are instilled thrice daily, the most suitable preparations being 10% lunosol or neoprotosil, or colossal argentum 1:2000 (CROOKES). After two or three days the inflammation commences to subside, and the intervals between successive irrigations may be lengthened and the silver solution applied twice a day, If there is a tendency for the palpebral conjunctiva to become granular in the later stages of the disease, lavage with astringent preparations such as nizin (zinc sulphanilate) 1:2000 or zinc sulphacarbonate 1:2000/

1•2000 is indicated. In cases in which bacteriological examination reveals a mixed infection, chloramine T 1•10,000 to 1•5,000 should replace the saline solution. At the earliest sign of commencing corneal involvement a few drops of atropine solution (½ to 1%) should be instilled into the affected eye, and repeated bi-daily.

In cases of VULVOVAGINITIS the child derives considerable relief from pain and irritation from alkaline hot hip baths rendered antiseptic by the addition of a few drachms of lysol or "Sanitas". After a bath the child is placed on its back, and the vulvar surfaces cleansed with weak lysol or eusol. A Kidd's female urethral catheter, attached to a 20cc. glass syringe by means of a short piece of rubber tubing, is then introduced into the vagina, which is irrigated very slowly with a solution of 1:4000 to 1:2000 mercurochrome, 10% lunesol, or ½% aqueous picric acid. After withdrawing the catheter, a small medicated pessary containing ¼ to ½% picric acid, 1/8 to ½% mercurochrome, or 2½ to 5% lunosol, is inserted into the vagina. In some cases of vaginal infection it may be necessary to incise, or stretch the hymen, before vaginal lavage is possible. If the urethra is also involved it should be irrigated with the same solution that is used for the vagina, and

a/small

a small medicated bougie is left in the lumen. The Bartholinian glands and ducts which are not functioning in children are practically never infected. The vulvar surfaces are washed with the irrigating fluid, dried with gauze, and dusted with compound dermatol powder.

Not infrequently cases of vulvo-vaginitis are very difficult to cure; all symptoms and apparent signs of the disease subside yet gonococci are repeatedly found in the vaginal smears. In some cases this may be due to repeated reinfection from an unrecognised untreated urethritis. In resistant cases the vaginal mucosa and cervix uteri should be examined directly with the aid of a urethroscope and if necessary should be touched with stronger antiseptics such as 1 to 2% silver nitrate, or 1% aqueous solution of picric acid. In some cases benefit may be derived from injection of 1% mercurochrome paste into the vagina, or other solutions such as hydrogen peroxide(10-20 vols.) acriflavine 1:4000, albargin 1:4000, potassium permanganate 1:8000 to 1:6000, and chloramine T 1:5000, may be successfully used as irrigations.

GENERAL/

GENERAL TREATMENT.

Medicinal and dietetic treatment are only of value in so far as they influence the symptoms and course of focal disease in the genito-urinary system, and so benefit the joint lesions indirectly. Drugs used for the relief of pain in acute rheumatism such as the salicylates, and amidopyrine, strongly advocated by BODENSTAB (73) (1895) are useless as analgesics in gonococcal arthritis, and the calcium salt of ortho-iodoxy-benzoic acid, (a drug which will be dealt with in more detail in the section on chemotherapeutic substances) recommended recently for its beneficial effect in all types of infective joint lesions, has so far, proved of doubtful value in gonococcal cases. Novalgin (Bayer) in ½ gram.doses thrice daily, gives the best results in the relief of pain.

When acute genito-urinary lesions are present a simple diet is indicated with plenty of fluid, preferably plain water, milk, and barley water, between meals, and spiced foods, pickles, sauces, pepper or mustard, meat and alcohol are avoided. An alkaline diuretic and urinary sedative, containing sod.bicarb.grs.xx., sod.citrat.grs.xx. tinct. hyoscyam. Mxxx., infus.buchu 1 oz., is taken three or four times/

times a day. In cases of cervical, uterine and tubal infection in women, and prostatic and vesicular affections in men, tinct.bellad.M vii. is added to this mixture for its sedative action. If chordee is present in acute cases of seminal vesiculitis, this painful condition is relieved by taking camphor monotromate grs.v. to viii in cachets thrice daily or twice during the evening. In cases of acute gonorrhoea, methylane blue gr.i, combined with boric acid grs.iv. constitutes a valuable adjuvant to treatment. In chronic gonococcal arthritis when the general health is impaired and anaemia is present, tonics containing iron, strychnine and arsenic should be prescribed.

GENERAL/

GENERAL TREATMENT by the BLOOD STREAM.

Treatment by the blood-stream may be divided into therapy with vaccines, sera, proteins, and chemo-therapeutic substances.

VACCINE THERAPY.

So poor is the specific antibody formation following infection by the gonococcus, that an endeavour should be made in every case to stimulate the formation of anti-substances artificially by innoculation with vaccines. In 1907 WOLLSTEIN (74) showed by animal experiment that injection of dead gonococci produced specific agglutins, and complement deviating substances. Since that date vaccines have been used extensively in the treatment of all manifestations of gonorrhoea, and the literature on the subject is enormous.

In 1907 gonococcal vaccines were employed in the treatment of gonococcal arthritis by different observers with marked success. COLE & MEAKINS (75) reported results in 15 cases, ten being cured and 5 improved. OHLMACHER (76) treated 2 cases, one being cured and the other improved. The majority of observers who have written on vaccine therapy in the treatment/

treatment of gonorrhoea, are of the opinion that it is an invaluable therapeutic measure in cases of arthritis. In a review of 68 articles on the subject THOMSON (77) found excellent results reported in 66 of them; only two authors failed to note any benefit from the use of vaccines in joint lesions.

Of the many types of vaccines that have been employed in the treatment of gonococcal arthritis, I should like to draw attention to the following which have been used by different workers with varying degrees of success:;-

1. Ordinary polyvalent gonococcal vaccines.
2. Autogenous vaccines.
3. Sensitised vaccines.
4. Commercial stock vaccines, such as "Dmegon", "Arthigon", and "Staphgon".
5. Gonococcal Phylacogens.
6. Detoxicated polyvalent vaccines.

Differences of opinion exist as to the most suitable and effective variety of vaccine, the most favourable initial and subsequent dosage, and the best method of administration. I have only had experience of ordinary polyvalent gonococcal vaccines, autogenous vaccines, "arthigon" and detoxicated vaccines in the treatment of gonococcal arthritis.

A/

A polyvalent vaccine consists of an emulsion of dead gonococci of many strains. This type of vaccine was used by the earlier workers, and has been employed extensively since. It has been administered intravenously, intramuscularly and subcutaneously, and various initial doses have been suggested. As it is a toxic preparation, one should commence treatment with small doses of 5-10 million gonococci. The vaccine is given intramuscularly or subcutaneously, as the reactions following intravenous injection are liable to be severe. Subsequent dosage should be controlled by careful observation of the local, focal and general reactions. If the initial reaction has not been marked, a second injection of 10 to 15 million is administered four or five days later. Thereafter injections are given at intervals of five to seven days, gradually increasing the interval to ten days with larger doses. A moderate reaction with an increase in temperature of 1° to 1·5° F., is followed by the best therapeutic result. A course of 10 to 12 injections will usually suffice. Some authorities maintain that small doses at short intervals, give better results than large doses at longer intervals. As pointed out by ARONSTAM (78) 1908 no rule can be laid down as regards dosage, this depends upon the reaction in each individual case.

The/

The opsonic index of the blood is a useful guide to vaccine treatment. Its estimation has been advocated as a routine procedure in controlling dosage. It can best be estimated by WRIGHT'S (79) modification of Leishman's original method. When a medium dose of vaccine is administered there is an immediate slight fall (negative phase) in the opsonic index. This lasts 36 to 48 hours, and is followed by a rapid rise (positive phase). Following this rise there is a gradual fall to normal. With small doses of vaccine there is no negative, but only a slight positive phase of short duration. If too large a dose is given, there is a prolonged negative phase with slow recovery. To obtain the best clinical results, the second injection should be given as the positive phase reaches its height. Should vaccine be injected during the negative phase, a still greater and perhaps dangerous fall, will result. The examination of the blood in this way, however, is not to be recommended as a routine measure. Readings of the opsonic index, however accurately estimated, although useful, can reveal little that cannot be detected more easily by careful clinical observation. The technique of the test is by no means simple, and the results are somewhat indefinite; and not infrequently the opsonic index does not exactly follow the symptoms. BEGG (80) says, -

"When/

"When this happens, prefer to be guided by the clinical symptoms, for as someone has remarked, it is the patient's disease, not his opsonic index, that is under treatment".

Estimation of the opsonic index was carried out in a series of cases of gonococcal arthritis in 1908 by IRONS (81). Before vaccine therapy was commenced, it varied from 1 to 1·6; the average being 1·0, Vaccines produced a sharp rise to 2·5 or 3·0. He found that massage of the prostate and joints was followed by a rise, due he concluded to autoinnoculation.

BRUCK (82) (1912) maintained that it was useless to estimate the opsonic index during vaccine treatment. He pointed out that the leucocytes naturally ingested the gonococci, but that the latter were not damaged in any way by this active phagocytosis. In fact, the leucocytes and organisms lived together in a state of symbiosis. It therefore appeared to him illogical to base the administration of a vaccine upon the opsonic index, when it was well known that this power of the leucocytes already existed naturally to a maximum degree.

AUTOGENOUS/

AUTOGENOUS VACCINES.

Vaccines made from the patient's own infecting organisms are exceeding useful in the treatment of gonococcal arthritis. It is somewhat difficult to state whether autogenous are superior to ordinary polyvalent vaccines in this condition. Both are good antigens. Some workers including HARTWELL (83), MURRELL (84), and THOMAS (85), prefer autogenous vaccines, whilst others including BRUCK (86), McDONAGH (87), POLLOCK (88), and HARRISON, are of the opinion that gonococcal vaccines of high polyvalency give better results.

In cases where bacteriological examination of the primary focus of infection reveals mixed infection with other micro-organisms, an autogenous vaccine made from infected secretions, will prove of immense value. If the vaccine does not contain the gonococcus, its administration should be combined with a polyvalent gonococcal vaccine, preferably detoxicated. This combination is especially indicated in subacute and chronic cases, in which mixed infections are common. A suitable initial dose for an autogenous gonococcal vaccine is 5-10 million organisms. The second dose, of 10-15 million, is administered on the fourth or fifth day, and thereafter the dosage is increased so as to produce a slight tempera-

ture/

temperature reaction. As larger doses are given, the interval between them is lengthened.

The initial and subsequent dosage of a mixed autogenous vaccine, will naturally depend on the nature and strength of the organisms contained in it. The initial dose of the polyvalent gonococcal vaccine combined with it is 5-10 millions, or if detoxicated, 2500 - 5000 millions.

The mode of administration will vary in different cases. In out-patients subcutaneous or intra-muscular injections, which give rise to milder reactions, are preferable to intravenous. In patients with subacute and chronic arthritis, in whom large doses of vaccines are usually well tolerated, the intravenous, is the method of choice.

SENSITISED VACCINES.

A sensitised vaccine is one that has been subjected during its preparation, to treatment with its appropriate anti-serum. It is held that the process of immunization is hastened in this way, by performing the first stage in vitro.

The use of a gonococcal vaccine, sensitised by Besredka's method, was strongly advocated in the treatment of gonococcal arthritis, by CRUVEILHIER (89) in 1913. He found it especially valuable in acute cases/

cases; pain was readily abolished, and full range of movements restored, after four or five injections. In certain cases better results followed the use of a living rather than a dead sensitised vaccine, and he preferred a sensitised stock vaccine, made from material several months old to a sensitised autogenous vaccine. Reactions following injection of sensitised vaccines are of a mild character.

DOPTER & PAURON (90) (1913) also obtained rapid cures with sensitised vaccines, their results being superior to those obtained by any other treatment.

BROUGHTON-ALCOCK (91) (1913) used this type of vaccine with good results especially in acute cases, the pain being alleviated within 48 hours, and the swelling disappearing within three days. He considered that living sensitised gonococci were no better than dead sensitised vaccines.

McDONAGH & KLEIN (92) obtained better results with a vaccine sensitised with human anti-gonococcal serum, than with onesensitised with immune horse serum.

In 1918 HOWARTH (93) reported 16 cures, out of 17 cases of acute and subacute gonococcal arthritis, treated with sensitised vaccines. At first he used autogenous, but later found that stock vaccines made from four strains of fresh gonococci, gave the best results/

results. He avoided using gonococci that had been subcultured for more than four months.

In 1915 KAKEHI (94) showed by immunising experiments in animals that sensitised vaccines were less toxic than non-sensitised vaccines.

On account of their reduced toxicity, sensitised vaccines can be administered in larger doses than ordinary polyvalent, or autogenous vaccines. BROUGHTON-ALCOCK advised 500 million organisms as an initial dose, increased to a maximum of 3000 million. HOWARTH, at first commenced treatment with 25 million gonococci but later, finding that larger doses were tolerated, gave 100 million initially, increasing by 200 million every fourth day, according to the reaction, to 2000 million as a maximum.

COMMERCIAL STOCK VACCINES.

(1) "Dmegon".

In 1913 NICOLLE and BLAIZOL (95) introduced a new gonococcal vaccine under the name of "Dmegon", which they claimed was non-toxic and could be adminstered in large doses. The reduction in toxicity was obtained by growing the gonococci in a special medium containing meat broth, urea, glucose, phosphate of ammonia and agar, to which rabbit serum had been added. The growths were emulsified in .7% sodium fluoride solution , and repeatedly washed and centrifuged in this solution. This process they claimed prevented autolysis and lessened toxicity. To this was added a Gram-positive coccus ("synococcus"), frequently associated with the gonococcus, in the proportion of one part of gonococcus, to nine parts of "synococcus". The initial dose was .5 c.c. containing 25 million gonococci, and 225 million "synococci", administered intramuscularly, diluted with 1.5 c.c. of saline solution.

Favourable clinical results in gonococcal arthritis were reported by NICOLLE and BLAIZOT, and other French workers, but the vaccine has never been/

been used to any extent in this country.

(2) "Arthigon".

"Arthigon", a commercial German polyvalent gonococcal vaccine, containing urotropine, first used with marked success in the treatment of gonococcal arthritis by ROHRBACH (96) 1912 and DORN (97) 1912, has proved a useful vaccine in the hands of many clinicians. In the opinion of BRUCK (98) (1912) "Arthigon" admirably replaced autogenous vaccines, which always require time for their production, and was superior to other vaccines.

BARDACH (99) (1913) also obtained good results in arthritis by intravenous injections of "Arthigon", preferring large to small doses; FREUND (100) (1913) regarded the vaccine as a specific remedy in gonorrhoea, and reported excellent results from its use in acute arthritis.

HAGEN (101) (1912) however was not impressed with results following its administration, and failures were reported by ROTH, KLINGER and OPPENHEIM (102) (1913).

HABERMANN (103) (1914) noticed an extension of arthritis during "Arthigon" treatment and pointed out/

out that other observers (ROTH, FOCKLER, and MENZER) had noticed also, the occurrence of complications during treatment. He concluded that the clinical improvement following intravenous injections of "Arthigon" was no better than that which resulted from the hypodermic injection of ordinary vaccines.

In my series of cases, fourteen were treated with intravenous injections of "Arthigon". Of these eleven had acute, and three chronic arthritis. Of the former six were cured, and five were definitely improved. Of the latter, one was cured, and two showed improvement. No case failed to derive some benefit. In all cases the local and focal conditions received simultaneous treatment.

Patients are best treated in hospital. An initial dose of ·05 c.c. or ·1 c.c. (100 million organisms are contained in 1 c.c.) is administered intravenously and a second injection of ·15 c.c. or ·2 c.c. given on the fourth day. Thereafter the dosage is increased by ·05 c.c., ·1 c.c., or ·2 c.c., according to the reactions to a maximum of 1 c.c., the interval between injections being lengthened with larger doses.

After/

After the first two or three injections fairly marked general reactions are liable to occur. About 20 to 40 minutes after an injection, shivering sets in, the patient feels ill, joint pains are increased, and there is headache which may last for 2 to 4 hours. The temperature rises sometimes to 102°F. With subsequent injections reactions are less marked and frequently absent, unless, of course the dosage is increased too rapidly.

In my opinion "Arthigon" administered intravenously is of decided value in the treatment of gonococcal arthritis, especially in the acute and subacute stages when X-ray examination reveals negative proliferative and degenerative changes in the affected joints. "Arthigon" benefits the associated genito-urinary infection, as well as the arthritic condition, and in the cases treated, with positive urethral smears, gonococci rapidly disappeared from the discharges.

(3) "Staphgon".

LUMB (104) (1917) reported excellent results in ten cases of gonococcal arthritis treated with a mixed stock vaccine, called "Staphgon", containing

50/

50 million gonococci and 150 million staphlococci per c.c. Staphlococci are so often associated with gonococci in infections of the genito-urinary tract that he assumed that results superior to those obtained with a pure gonococcal vaccine would follow the exhibition of a mixed vaccine of this nature. At first he commenced treatment with a dose consisting of 5 million gonococci but finding that larger doses were tolerated, raised the initial dose to 50 million gonococci and 150 million staphlococci. He advised the following course:-

1st day	1 c.c.	= 50 mill. g.c. and 150 mill. staphs.	
3rd "	2 c.c.	= 100 " " " " " "	
6th "	"		
9th "	"		
12th "	"		
15th "	"		

The vaccine was then discontinued for ten days, after which a second course, such as the following, was recommended.

25th day	2 c.c.	)100 mill. g.c. & 300 mill.staphs.
28th "	"	)
31st "	"	)
34th "	"	)
37th "	"	)
40th "	"	)

The ten cases were cured in an average of fifty days.

GONOCOCCAL "PHYLACOGEN"

Believing that every bacterial infection is the result of a mixed infection, A.F. SCHAFER (California) placed on the market a propietory preparation of bacterial filtrates under the name of "Phylacogen". A basic "Phylacogen" consists of a mixture of filtrates (through porcelain) of cultures of staphlococcus pyogenes (albus, aureus, and citreus) Streptococcus pyogenes Bpyocyaneus, diplococcus pneumoniae B.typhosus, B.coli, B.diphtheriae streptococcus rheumaticus and streptococcus erysipelas, A gonococcal "Phylacogen" is prepared by mixing together equal parts of this "Mixed Infection Phylocagon", and the filtrate of a pure culture of gonococci. This preparation contains no solid bacteria; it is hot a vaccine but a bacterial filtrate, and is more analagous to the toxins used in the manufacture of antitoxins, Subcutaneous administration is recommended, commencing with a dose of 1 to 2 c.c., and increasing by 1 to 2.c.c. until a maximum of 10 c.c. is reached. If used intravenously treatment is commenced with doses of ·125 c.c. to ·25 c.c. gradually increasing to a maximum of 5 c.c. avoiding/

avoiding marked general reaction. Injections are given every 24 to 48 hours.

In order to test the therapeutic value of gonococcal "Phylacogen" HARRISON (105) (1913) treated 16 cases of gonorrhoea, including one case of polyarthritis. He concluded that the preparation hastened recovery, and rapidly banished pain in gonococcal arthritis, but was useless in the treatment of other manifestations of gonorrhoea. Large doses were more useful in diminishing pain than small ones. This was due, HARRISON believed, to the febrile reaction produced. He also tested the antigenic power of "Phylacogen" in the complement-fixation test, and found that it did not act as a good antigen, being inferior in this respect to an ordinary emulsion of gonococci.

DETOXICATED GONOCOCCAL VACCINES.

In 1917, D. THOMSON (106) described a method by which it was possible to separate gonococci from their toxins. When treated with normal NaOH, the organisms dissolved, and when the solution was rendered acid by normal HCl, a gonococcal protein was precipitated. This precipitate was found to be about fifty times less toxic than the original gonococci, and/

and the toxins removed were present in the supernatant acid solution, which could be filtered from the "non-toxic" precipitate. The precipitate although less toxic than the original micro-organisms, was found by animal experiment, and by the complement-fixation test, to have retained its antigenic properties. The importance of this discovery lay in the fact that vaccines treated in this manner, being less toxic, could be administered in very much larger doses than was possible with non-detoxicated vaccines, and therefore they were superior in immunizing power.

It was soon found that this simple process would not suffice, because it became evident that the precipitate obtained did not represent the entire "non-toxic" part of the germ substance, as other "non-toxic" constituents existed in the toxic supernatant fluid.

In 1921, THOMSON evolved a new method of detoxication, whereby he was able to recover other "non-toxic" fractions, which were either alkali, acid, water, alcohol, or chloroform soluble; and each of these he found possessed antigenic properties. He discovered also that in the first stage of the process unaltered organisms, that had escaped the solvent/

solvent action of the alkali, were invariably present in the precipitate. To obviate this he passed the solution of each germ constituent through a Cumberland filter before precipitating it. In this way he was able to render the precipitate ten times less toxic.

Certain objections to the detoxication of vaccines have been raised by various authorities. It was contended that anti-substances could not be produced in the body by a non-toxic substance, because no reaction followed its injection. I quote THOMSON's reply to this; "Sheep cells", (red blood corpuscles), he points out, "are non-toxic to the rabbit, yet they induce most successful anti-substance formation. Sheep cells are 2000 times less toxic than the least toxic vaccine, so far produced, so that if we detoxicated germs 1000 times more effectively than at present, they should be capable of producing potent anti-substance when injected".

Secondly it was held that removal of toxins was unsound, because they are antigenic and stimulate antitoxins when injected, and produce reactions which

are/

are essential for successful antibody formation.

THOMSON summarises his argument against this contention as follows;

"(1) Antibodies are only produced against highly complex proteins.

(2) Antibodies are not produced against the simple disintegration products of proteins, such as amino-acids, etc.

(3) The toxic substances removed from germs by the author's process are very simple nitrogenous protein products, since they are soluble in alcohol. This is sufficient to show that these simple toxic products are of little value in immunity.

(4) The toxic products do not act antigenically when used in the complement fixation test.

(5) These simple toxins are not to be compared with the true exotoxins, such as the toxins of diphtheria and totanus bacilli. These latter true toxins are precipitated by alcohol. They are highly complex protein substances like snake venoms, and antitoxins are produced against them.

true

(6) Very few germs contain highly complex protein toxins.

(7) The simple toxins are very poisonous and harmful to the system, and should not be injected when they are of no antigenic value.

(8) When we aim at getting immunity towards a germ, we wish to get an anti-substance which will kill the bacterium rather than an anti-substance which will only neutralise its poison. For example, if we are defending ourselves against venomous snakes, it is surely better to kill the snakes outright, rather than to attempt to render them harmless by removing their venom sacs only.

(9)/

(9) A reaction does not per se produce any antibody. For example, intense reactions can be produced by injecting absolute alcohol or other such irritants under the skin, but no antisubstances are produced against these irritants."

It was argued also that the specific antigenic value of the germ proteins is destroyed during the process of detoxication; but THOMSON points out that, "the detoxicated germ substance still remains a good antigen when used in the complement-fixation test. Moreover, sheep cells when put through the same process are still capable of producing haemolysins when injected into a rabbit: vide BALLS and KORNS (107) (1918). Tissue cells when put through the process, are capable of producing specific cytolysins when injected into another species of animal; vide KOLMER (108) (1917)".

Detoxicated gonococcal vaccine, as prepared by THOMSON has met with marked clinical success, and is used as a routine in the treatment of gonorrhœa and its complications in the Venereal Diseases Department of the Royal Infirmary, Edinburgh, and in many other V. D. clinics. It cuts short the disease, diminishes the liability to complications, and any reactions that occur are of the mildest type. In gonococcal/

gonococcal arthritis it is of especial value, and the clinical results following its administration are excellent.

This vaccine may be given intravenously, intramuscularly or subcutaneously. Clinical trial has shown that the intravenous route has no advantages over the intramuscular or subcutaneous method of administration except perhaps in chronic cases. In acute arthritis therapy is commenced with an intramuscular injection of 2500 to 5000 million gonococci. After an interval of four to five days, 5000 to 7500 millions are given, and five or six days later 10,000 millions. Thereafter, according to the clinical reaction, the dosage is increased by 5000 millions weekly, to a maximum of 30 to 50,000 millions. It is not advisable to administer a vaccine on the same day that prostate massage is carried out, because a varying degree of auto-innoculation follows the latter.

When a mixed infection of the primary focus is present, it is advisable to combine the vaccine with an autogenous vaccine containing all the secondary organisms. If this latter is detoxicated

by/

by THOMSON's method, dosage, similar to that of the detoxicated polyvalent vaccine, is followed. In these cases with mixed infection good clinical results have been obtained by exhibiting a detoxicated stock vaccine of secondary organisms prepared by the same method. In each c.c. this vaccine contains gonococci 25,000 millions, staphlococci 5000 millions, streptococci 5000 millions, C. Xerosis and Hofmannii 5000 millions, enterococci 5000 millions and B coli 5000 millions. The dosage is similar to that of the detoxicated gonococcal vaccine.

In early acute cases of gonococcal arthritis the initial dosage of vaccines can be greatly increased, with little risk of producing a negative phase, by preliminary desensitisation. A small dose of detoxicated vaccine containing 500-1000 gonococci is administered intravenously, and half an hour later when the patient is completely desensitised to the organisms, a massive dose of 25,000-30,000 millions, can be injected intramuscularly or subcutaneously with safety. If an ordinary polyvalent vaccine, non-detoxicated is used, the desensitising dose contains 50-100 organisms, and is followed after the same interval by 500-1000 millions, administered intramuscularly or subcutaneously.

Thereafter/

Thereafter the large doses can be suitably increased at varying intervals of a week to ten days.

D. LEES (107) 1919 referring to therapy with detoxicated gonococcal vaccine states, "It is the most logical, scientific, and effective way of treating gonorrhoea and its complications, ... no other form of vaccine, sensitised or otherwise prepared, and no phylacogen, produces such rapid and great specific reactions unless used in toxic doses".

SERUM THERAPY.

During recent years anti-gonococcal serum has not been employed very extensively in the treatment of gonorrhoea. From the results obtained by workers in the past it must be admitted, however, that although of little value in uncomplicated cases of gonococcal infection of the urethra, it is of use in certain complications, especially arthritis.

In a review of 50 articles on the subject THOMSON (101) found that 43 authors considered that antigonococcal serum was of some therapeutic value, while only five, or 10%, believed it to be of no value whatsoever.

Antigonococcal serum was first used in the treatment/

treatment of gonococcal arthritis by TORREY[111] (1906) who reported cures in acute cases. He administered a serum prepared by RODGERS[112] (1906) in doses of two to six c.c. subcutaneously at intervals of 48 hours to seven days. In 1907 RODGERS and TORREY[113] recommended the use of a polyvalent antigonococcal serum prepared by injecting many strains into rabbits; eleven cases of arthritis were treated and all were cured with three or four injections. The serum was injected in 2 c.c. doses subcutaneously into the upper arm every other day.

TORREY[114] (1907) published results of 70 cases of gonococcal arthritis treated with this serum; 78% were entirely cured or much improved. Twenty were cured in ten days or less after an average of five injections. PORTER[115] (1907) claimed rapid cures in all six of his cases.

HERBST[116] (1908) however, obtained little improvement in acute cases, but all chronic cases showed distinct improvement after the first few injections.

Since 1908 antigonococcal serum has been tried by a number of clinical workers. Some have obtained good results, while others considered the serum/

serum to be valueless as a therapeutic agent. BALLENGER[117] (1909) had 72% of cures in 90 cases of gonococcal arthritis, but in the hands of FLETCHER[118] (1909) and BRUCK[119] (1909) serum therapy was a failure.

THOMAS[120] 1910 considered anti-gonococcal serum onlu useful in cases of chronic arthritis . LOUIS[121] (1910) and STELLWAGON[122] (1910) were favourably impressed with specific serum therapy in gonococcal arthritis. In 1914 CORBUS[123] reported results of eight cases treated with large intramuscular injections of anti-gonococcal serum (P.D. & Co) There was rapid improvement in four acute cases, but one relapsed. In four chronic cases one showed marked improvement (36 c.c. given) and three showed slow improvement (18 c.c. given)

In 1919 DEBRÉ and PARAF[124] drew attention to the value of intra-articular injections of a polyvalent anti-gonococcal serum. They maintained that the serum, to be efficacious, should be brought into immediate contact with the microbe, as is done in the treatment of cerebro-spinal meningitis by intra-thecal injection. Of 15 cases treated, six were completely cured in less than eight days; eight others were/

were cured before the 15th day, and one derived no benefit. The effusion was aspirated from the affected joints, and serum injected. This procedure was repeated at intervals of one to three days. In six cases of polyarthritis all the joints involved were treated at the same time. These writers stated that local serotherapy has to be supplemented by intramuscular or intravenous injection of the anti-serum in order to produce a general immunity and to prevent involvement of other joints. As it is practically impossible to inject the anti-serum into small joints, the treatment is limited to the larger joints.

Antigonococcal serum was not used in any of the cases I have studied. Although many workers have obtained considerable improvement and cures from serum therapy in gonococcal arthritis, it is clear that antigonococcal sera cannot replace vaccines in the treatment of this condition. THOMSON advises specific serum therapy in those resistant cases that fail to respond to other treatment.

Serum-therapy, moreover, has distinct disadvantages. Not only is there considerable pain and discomfort and sometimes urticarial rashes after intramuscular and subcutaneous injection, but there is/

is always the danger of anaphylaxis at some future date, when injection of some other antiserum may be necessary, as in the event of diphtheria etc. "The previous injection of serum may be the cause of anaphylactic shock, which might jeopardise the patients life when a well recognised antiserum is indicated and injected". (THOMSON)

It is interesting to note that certain workers here obtained good results in the treatment of gonococcal arthritis from the injection of non-specific sera. In 1906 SOLTAN, FENWICK and PARKINSON (125) reported rapid cures by the rectal administration of anti-streptococcal serum. These results were supported by FOX (126) (1906) and SALTER (127) (1910) the latter recommending an injection of a polyvalent anti-streptococcal serum, per rectum, in doses of 10 c.c. repeated on two successive days. CAMPBELL WILLIAMS thought that these results supported the view that gonorrhoea was a mixed infection. The therapeutic benefit derived from the serum in these cases was probably due to protein shock.

Antimeningococcal serum has also been used with success in the treatment of gonococcal arthritis. CHIARI (128) (1914) states that in a review of the literature on this condition he found reports of sixteen cases treated with antimeningococcal serum, with/

with thirteen cures. In 1916 MALLETERRE (129) reported successful results from the use of this serum in gonococcal arthritis. It is possible that this serum may be of value because of the similarity between the meningococcus and gonococcus. THOMSON points out that the complement-fixation test reveals this close relationship very clearly. The serum of a person suffering from cerebrospinal meningitis gives a positive complement-fixation reaction with a gonococcal antigen, and vice versa, a meningococcal antigen very often gives a positive reaction with the serum of a gonococcal patient. Hence it is possible that an antimeningococcal serum may have a beneficial influence in gonorrhoea. The same probably applies to meningococcal vaccines because in 1917 CALVER (130) found that they were just as useful in the treatment of gonorrhoea and gonococcal arthritis as gonococcal vaccines. He treated thirteen cases with injections of 100 millions gonococci and fifteen with injections of a similar number of meningococci, administering the vaccines at intervals of four or five days by the intravenous route. The therapeutic results and constitutional reactions were identical in the two series As he obtained similar results in seven cases treated on the same lines with intravenous injections of 25 million/

million B coli (100 millions gave rise to very severe reactions) he concluded that gonococcal vaccines are not specific, but that the clinical benefit runs parallel with the fever, and the hyperleucocytosis produced.

AUTOSEROTHERAPY.

Autoserotherapy is reported to give good results in gonococcal arthritis. In 1921 RAMOND (131) obtained cures in five severe cases by aspirating fluid from the affected joint and injecting it subcutaneously near the articulation. He injected 1 to 5 c.c. and repeated the procedure on several occasions. MAILLET (132) reported similar results, and CONSTANTINESCU (133) recorded successful results in cases of hydrarthrosis.

In 1921 BALLENGER and ELDER (134) strongly advocated autoserotherapy in the treatment of acute gonococcal arthritis, basing their views on an experience of 27 cases. Clear, non-infected synovial fluid, free from pus cells, was valueless, and unsatisfactory results followed its use. The aspirated fluid to be effective must be cloudy and contain pus cells, and the presence of micro-organisms adds to its success/

success as a therapeutic agent. As much fluid as possible (the amount varying from 15 to 50 c.c.) is withdrawn from the affected joints, and injected into the gluteal muscles. These authors maintain that injection into muscular tissue is better than into subcutaneous tissue, because of the greater resistance to organisms, and there is consequently less risk of abscess-formation. General reactions following injections were mild or absent, and scarcely any pain, no induration, and no suppuration supervened locally. Since employing this method these workers have found it unnecessary to resort to any treatment such as vaccines, sera, local applications, fixation, vesiculotomy etc.

DUFORE THIERS and Mlle. ALEXEWSKY (135) (1922) reported cures in six cases treated by this method. They state that pain and swelling soon abate, and that cures were obtained in from four days to one month. They emphasize the benefit to infective foci elsewhere in the body and the absence of local and general reactions. Even after the injection of fluid containing living gonococci, no abscesses followed.

Other workers who have had experience with this method of treatment in gonococcal arthritis with/

with effusion, are not so enthusiastic in recommending autoserotherapy as the authors I have mentioned. THOMAS (136) (1927) states, "I have never observed any notable advantage derived by injecting the patient intramuscularly with his own aspirated synovial fluid".

PROTEIN/

PROTEIN THERAPY.

It is an established fact that the resistance of the body to gonococcal infection can be increased, not only by the injection of specific vaccines, but also by the administration of foreign proteins. This reaction is a biological response, the exact nature of which is unknown. Many theories have been suggested, but it seems probable that no single factor can explain all the changes that bring about this immunising response. It is held by some that pyrexia is the main factor, the rise in temperature either destroying the gonococcus, which we know from clinical and experimental observations is thermolabile, or causing a more rapid and firm union of antigen and immune body. ROLLY and MELTZER[137] (1908) and LUDKE[138] (1909) and numerous other workers, found that a temperature of 104° to 107°F., artificially produced, had a favourable influence on an established infection, and agglutinins and bacteriolytic substances were produced more abundantly in animals which were kept overheated. KYAU[139] (1912) cites the work of FINGER and others who regularly failed to produce gonococcal urethritis/

urethritis experimentally in patients who had a temperature of 102·2° to 104°F. due to some existing disease, and CULVER[140] (1917) records a case in which an acute gonococcal urethritis was cured in four days by pyrexia following a relapse of malaria.

PETERSON and JOBLING[141] (1914) however, believe that there are other factors at work besides fever. They found that intravenous injections of non-specific substances in animals were followed almost invariably by an increase in proteose and lipase in the serum . Similar reactions occurred in patients after intravenous injections of vaccines and proteoses , though to a less degree and with much less regularity than in animals. They observed improvement in cases of established infections, following such injections, and suggested that the ferments might digest the microbes and toxins. They also found that the injections caused a transient decrease in the antiferments of the blood (perhaps due to the augmented metabolic demands in pyrexia) followed by a distinct & much more lasting increase. PETERSON and JOBLING[142] (1916) cite the work of DUMKLIN who used proteose injections in typhoid immune rabbits and found a decided increase in the antibody titre, which is/

is explained by a selective stimulation of the haemopoietic system by a non-specific protein.

A large number of different proteins have been employed from time to time in the treatment of gonococcal arthritis. Those most commonly used at the present day are non-specific vaccines especially typhoid vaccine, horse-serum, peptone,, sterile milk, and "Aolan" a proprietory preparation of sterile lact-albumen.

Non-specific proteins are erratic in their action, and do not give such consistently good results as specific vaccines. They are inferior to detoxicated gonococcal vaccines in the treatment of arthritis but it must be admitted that in some cases most striking clinical and bacteriological improvement follows their administration. "Aolan" and "sterile milk" are preferable in acute cases, as the reactions they give rise to are less than with any of the others, yet the therapeutic results are as good. "Aolan" is given intramuscularly in doses of 5 c.c., or intradermally in small doses of .3 c.c. In cases of subcute and chronic arthritis the best results follow the use of peptone or T.A.B. vaccine. Treatment with Armour's 20% peptone is commenced with an/

an intradermal injection of •2c.c. A week later •25 c.c. is injected intravenously. On the fourteenth day •3 c.c. is given and the dose increased weekly by •1 c.c., according to the reaction, to a maximum of 1 c.c. The initial dose of T.A.B. vaccine is 100 millions intravenously, and repeated every six days until six injections have been given, the dose being gradually raised to 200 or 250 million organisms. Reaction begins within an hour with a rigor and a rise in temperature to 103° to 105°F, followed by uncomfortable heat, then profuse perspiration, and return to normal, the whole reaction lasting from 6 to 12 hours. Focal reaction with pain in the joints is also marked, and there may be herpes at the mouth and slight albuminuria.

If milk is used, it is sterilised by boiling, allowed to cool to room temperature, and then 5 c.c. are injected into one or both buttocks, avoiding blood vessels.

In subacute cases which are not responding as well as might be expected to specific vaccine therapy, it is advisable to interpose injections of a suitable/

suitable protein between successive doses of vaccine. The joint exhibition in this way of specific vaccines and non-specific proteins will often clear up many resistant cases. In chronic cases a course of protein-therapy followed by vaccines gives better results than either proteins or vaccines alone.

CHEMOTHERAPY/

C H E M O T H E R A P Y.

Since Harrison in 1916 tried the effect of intramuscular injections of succinamide of mercury in the treatment of gonorrhoea and its complications, a large number of chemotherapeutic substances have been recommended by McDONAGH and other authors. It is generally admitted however, that although most striking clinical results occasionally follow chemotherapy, the drugs are notoriously uncertain in their action, and for consistently good results cannot be compared with detoxicated gonococcal vaccines. Amongst those chemical products recommended by McDONAGH for intramuscular administration are the following:- colloidal palladium, colloidal manganese, trimine (a mixture of iron, manganese, and zinc) intramine (a sulphur compound), manganese buturate, contramine (diethylamine carbon disulphide), and more recently amino-benzoyl-1-amino-8-naphthol-3-6-sodium sulphonate), "sup 36" (the symmetrical urea of para-benzoyl-para amino-benzoyl-1-amino-8-naphthol-3-6-sodium sulphonate), and "sup 468" (the symmetrical urea of para/

para-benzoyl-para-amino-benzoyl-1-naphthglamine-4-6-8-sodium sulphonate), and intravenously, auramine (a di-phenyl methane dyestuff).

Mercurochrome 220 given intravenously has been extensively used in America, and acriflavine has been strongly recommended for intravenous use by French workers. HERROLD and CULVER (141) (1927) recommend neutral acriflavine as an internal antiseptic and urinary sedative, administered orally in keratin coated tablets in dosage of ½grain, three times daily.

In gonococcal arthritis McDONAGH (142) (1928) advises the intramuscular infection of contramine to supplement vaccine therapy. In acute cases four infections of ·125gm. are given on alternate days, followed by four small doses of vaccine, and then contramine and vaccine injections are continued on alternate days until a cure is obtained. In chronic cases, two or three injections of contramine each of ·25gm. should be made at five day intervals. In cases with septicaemia, auramine is administered intravenously on two successive days in ·1gm. doses, and "sup 468" intramuscularly in ·001gm/

.001gm. doses until the patient recovers.

He states that "Sum 36" and "Sup 36" are also valuable drugs for raising the general resistance of the patient. The former is given in doses of .002gm. at five day intervals for three injections prior to the exhibition of vaccines, and the latter in doses of .01gm. According to McDONAGH (143) these drugs act by"conveying electrons to the protein particles (host's protective substance) which have been robbed of the same by the microbic invasion. Vaccines act by breaking up the enlarged and clumped protein particles, thereby restoring them to the circulation, with an increased negative charge, and Brownian movements. Therefore, for a vaccine to be efficient the bodies of the bacteria must be subdivided into as tiny particles as possible, because the smaller the particles become, the greater their negative charge, and enlarged protein particles can be broken up only by such charged particles. If the particles of the vaccine are not small enough they still further increase the size of the host's protein particles and occasion what is known as a "negative/

"negative phase."

He states that "Sup 36" is invaluable in all acute inflammatory lesions, and is superior to manganese butyrate.

YOUNG (144) and his co-workers have obtained good results from the intravenous injection of mercurochrome 220. It is administered every 48 hours in doses of 10cc of a 1% solution prepared by dissolving the granular form in warm, freshly distilled, water. Of the cases of gonorrhoea and its complications that they treated, 60% were cured. YOUNG states that failures have followed either insufficient treatment, or cessation of treatment on account of the early development of reactions.

BRAASH and BUMPUS (145) (Mayo Clinique) believe that mercurochrome is too toxic a preparation for routine administration. In their experience severe reactions narked by prostration, chills, and diarrhoea, were common, and two of their patients died.

According to WOLBARST (146) (1928) the drug is excreted in large quantities by the kidneys, and also secreted through theprostate, seminal vesicles and other glands of the genital tract. It therefore comes/

comes in direct contract with the affected areas through the blood stream and the urine.

LEES[147] (1927) states that his experience of mercurochrome 220, given intravenously, does not confirm the published work in America on this subject.

POTTER and REDEWILL[148] (1926) maintain that mercurochrome should always be administered in glucose solution, which activates the dye, and while increasing its efficiency as a therapeutic agent, reduces to a minimum, the risk of reactions. They advise an intravenous injection of 10cc. of a 1% solution of the drug in 50% glucose, followed immediately by an intramuscular injection of 5cc. sterile milk, the double injections being given every 48 hours. WILLIAMS and COOPER[149] have obtained good results with this method, but in place of sterile milk they advise the intramuscular injection of 5cc. of a mixture of condensed milk 250pts., water 250pts., glucose 50pts., and lactose 50pts., sterilized in autoclave.

Acriflavine is administered intravenously three/

three times a week in doses of 5cc. of a 2% solution in distilled water.

Acriflavine and mercurochrome given intravenously become diluted to such an extent in the body fluids that good results reported from their administration cannot be attributed to a bactericidal action. Such a doubt is expressed by the LANCET (150) in commenting on some experiments of COLEBROOK and HARE (151) which go to show that the intravenous injection of mercurochrome does not raise the bactericidal power of the blood. DALE (152) has made a study of chemotherapy with these drugs, and suggests the following possibilities of their method of action:- "That they do not kill the parasites immediately, but modify their virulence, or lower their resistance, to the body's natural defences; that they form in the body some-directly toxic products, either by modification of its structure, or by its union with some tissue component; and that they have an affinity for certain cells of the host's body, leading to the formation of a depôt from which the curative substance is relieved."

In/

In my experience chemotherapeutic substances are only to be recommended in the treatment of gonococcal arthritis as adjuvants, and not to the exclusion of specific methods of increasing body resistance to the gonococcus. In some cases which are not responding satisfactorily to vaccine therapy, an intramuscular injection of .25gm of contramine, or, an intravenous injection of 20cc. of 10% sodium iodide solution, between successive injections of vaccines, is often of considerable value in hastening recovery, especially if there is a tendency to the formation of fibrous adhesions in and around the affected joints. I have seen great benefit follow the use of sulfarsenol in acute cases where joint pain was a marked feature. It is a "914" organic arsenical preparation, and in these cases is administered intravenously in doses of 18-24ctgs. dissolved in 10cc. of doubly distilled water.

ORTHO-IODOXYBENZOIC ACID.

This drug should also be added to the list of chemotherapeutic substances used in the treatment/

treatment of gonococcal arthritis, although it has been employed more extensively in other types of arthritis, and with more favourable results. Ortho-iodoxybenzoic acid, ($C_6H_4(IO_2)COOH$,) first prepared by MEYER[153] in 1892 has been strongly advocated by YOUNG and YOUMANS[154] (1926) and others, in the treatment of different varieties of infective arthritis especially in the acute and subacute, but also in the chronic stages. YOUNG and YOUMANS published results of 43 cases, which included cases of acute, and chronic gonococcal, hypertrophic, and atrophic arthritis. Some of their patients were hopeless cripples in whom all other forms of therapy had failed; 56% were markedly improved, 23% moderately improved, 14% slightly improved and 7% derived no benefit from the treatment.

The drug resembles salicylic acid $C_6H_4(OH)COOH$, with the difference that the hydroxyl (OH) group, is replaced by an iodoxy (IO_2) group. The ammonium salt is administered intravenously in doses of ·75 to 1gm., dissolved in 100cc. distilled water or sterile saline solution. The fluid is allowed to enter the vein slowly by gravity and is followed/

followed by a small amount of saline solution to minimize contact with the walls of the vein. A course consists of 5 to 10 injections given bi-weekly. Although the intravenous injection is recommended as the method of choice, it appears that oral and rectal administration are also efficient. The calcium salt, which is preferable as it produces less irritation, is given by the mouth in capsules containing 1·5 gms., and the ammonium salt, 1 to 1·5 gms. in 2% solution, is given rectally, after a cleansing enema.

MILLARD SMITH (155) (1927), from an experience of the drug in 33 cases of arthritis, states that that the special indications for its use are pain, swelling, and muscular spasm, and advises it in all cases of arthritis, of whatever nature, presenting any of these three symptons. He asserts that analgesia comes on ten minutes after the injection, and lasts for 24 to 48 hours, and the patient may be completely relieved of all pain; and muscular spasm disappears in from 6 to 12 hours.

STEIN and TRAUBE (156) (1928) report results in 102 cases of arthritis including two cases/

cases of gonococcal arthritis, treated by this method. On account of very severe reactions, that occurred in 82 cases, and poor results generally, they decided to discontinue the use of the drug. Intravenous injections in the gonococcal cases, produced no appreciable improvement.

MILLARD SMITH (157) (1928) however, is of the opinion that the severe reactions and inferior results obtained by these authors, were probably due to the fact that in patients troubled with constipation and indigestion, treatment invariably fails and reactions are common. Until these conditions are corrected little improvement is to be expected.

MENACE (158) (1928) reports a death occurring seven hours after an intravenous injection of the ammonium salt, and states that the drug must be used with the utmost caution. YOUNG and YOUMANS refer to the frequent occurrence of venous thrombosis in their early cases. Substitution of the ammonium for the sodium salt has lessened, but not entirely prevented, this risk.

It is stated that O-iodoxybenzoic acid

and/

and its salts have a similar action to salicylates but are more potent drugs. In view of the fact that salicylates are useless in the treatment of gonococcal arthritis, and that very severe and even fatal reactions may follow injection of the acid and its salts, this method of treatment cannot, as yet, be recommended in cases of arthritis of gonococcal origin. Moreover, little or no clinical improvement has been observed in cases of gonococcal arthritis treated in this way. It is possible however, that as a result of further research, less toxic preparations of O-iodoxybenzoic acid of considerable therapeutic value, may be discovered.

CRITICAL/

CRITICAL COMMENTARY, based on a review 119 cases of gonococcal arthritis, with reference to,

a. DIAGNOSIS

b. PROGNOSIS

c. TREATMENT

a. DIAGNOSIS

Examination of the genito-urinary system for signs, symptoms, and bacteriological evidence of gonococcal infection, is the most important means of diagnosis in acute gonococcal arthritis. Arthritis, appearing in the course of acute gonorrhœa is invariably gonococcal in nature. The secretions of the urethra and prostate in the male, and of the urethra, bartholinian ducts, and cervix uteri in the female, are examined for the presence of the gonococcus by smear, or culture. If smears, stained by Jensen's modification of Gram's stain, are repeatedly negative, cultural examination should always be undertaken. In doubtful cases positive results by smear or culture are more often obtained if specimens are examined forty-eight hours subsequent to the intramuscular injection of a polyvalent gonococcal vaccine, containing 300 to 500/

500 organisms.

An acute infection of a joint which does not subside, when other joints are successively involved, is suggestive of gonococcal arthritis, and concomitant teno-synovitis is a feature of diagnostic importance.

Joint puncture is rarely necessary in establishing a diagnosis; the discovery of the gonococcus in the aspirated fluid is absolute proof of the arthritis being gonococcal, but a negative result, does not exclude this possibility.

Radiograms of the affected joints are of value in excluding acute infective arthritis due to virulent pyogenic micro-organisms.

The complement fixation test of the blood if positive, is diagnostic, if gonococcal vaccines have not been administered, but it is unnecessary in the majority of acute cases.

In subacute and chronic cases a diagnosis is made from similar observations supplemented by a careful search throughout the body for other causes of focal infection, and other conditions that/

that may give rise to chronic non-gonococcal arthritis. Examination of the blood by the complement-fixation test should never be omitted; the test is most valuable in those cases in which bacteriological evidence is lacking. . Radiograms are essential in eliminating other types of chronic arthritis, and the Wassermann test of the blood should always be performed to avoid overlooking a syphilitic ætiology.

b. PROGNOSIS.

The prognosis in acute and subacute cases is always good. If suitable local and general treatment, combined with treatment of the primary infection, is carried out, the inflammation usually subsides slowly, and resolution is complete; and adhesions and subsequent ankylosis, do not occur. A warning against future gonorrhoea must be issued, because of the great risk of arthritis recurring with subsequent attacks.

In the series under review there were 92 acute and subacute cases; 67 of these were cured. Twenty-four patients either ceased treatment or were transferred to other clinics; 23 of these were markedly improved, and one was slightly improved. One patient/

patient died during treatment from an intercurrent disease.

The prognosis in chronic cases is dependent on the degree of osseous, cartilaginous, and peri-articular involvement; the more pronounced the involvement is, the worse the prognosis and vice versa. The functional disability is usually permanent in cases with superadded changes of "rheumatoid" or chronic infective arthritis. There were 27 chronic cases in my series. Twelve of these were cured, 7 were markedly improved, and one was slightly improved; and seven cases ceased attending, after having derived slight benefit from treatment.

c. TREATMENT.

(1) Local Treatment.

For the relief of pain, immobilization of the affected joints, soothing local applications, and Bier's congestion, are the methods of choice. Electrical treatment with diathermy, continuous currents, or ionization with salicylates, does not give any more favourable results; but diathermy is a useful adjuvant to treatment. Massage and mobilization are commenced when the acute symptons have subsided, and at this stage mild counterirritation with stimulating ointments/

ointments such as capsicum and salicylic acid, and hot air baths, twice daily, are valuable in promoting absorption of inflammatory products. Intra-articular effusion usually subsides with Scott's dressing and other local measures; and joint puncture with aspiration of the fluid, is only indicated in cases with marked effusion, which persists, or tends to increase, in spite of other treatment.

Arthrotomy, with antiseptic lavage of the joint cavity, is unnecessary in the routine treatment of the average case, and is only called for in cases of pyarthrosis.

In chronic gonococcal arthritis the best results from conservative treatment are obtained by a combination of measures designed to relieve pain, promote resolution, and restore function in the affected joints. These include passive congestion by BIER's method, active hyperaemia by hot air baths and diathermy counter-irritation with stimulating ointments, such as iodex and methyl salicylate, and capsicum and salicylic acid, massage, and active and passive movement.

Scott's dressing is valuable in cases of hydrops articuli. Aspiration is rarely necessary unless/

unless the effusion is marked and does not diminish with other treatment.

Mobilization under general anaesthesia is indicated in cases of intractable arthritis, where limitation of movement is due to fibrous adhesions. It is contra-indicated when osseous ankylosis is present.

Radical methods such as arthroplasty and arthrodesis, are reserved for those joints that have been rendered useless on account of advanced degenerative and proliferative changes. In such cases little hope of success is to be expected from conservative treatment.

(2) TREATMENT OF THE PRIMARY INFECTION.

Treatment of focal infection in the genito-urinary tract and elsewhere, is a sine qua non in acute, subacute, and chronic cases.

a. FOCAL TREATMENT IN MEN.

In acute and subacute cases, urethritis, prostatitis, and vesiculitis, are usually present. If the arthritic symptoms are acute, and it is inadvisable to move the patient, focal treatment should consist of gentle irrigation of the anterior urethra, and the use of morphia or atropine and antefebrine, rectal suppositories. When the patient can be moved posterior irrigation, hot hip baths, and hot rectal douches are commenced, and continued twice daily. When gonococci are present in the urethral smear potassium permanganate 1:8000, preferably in alkaline solution, is the irrigation of choice. After seven to ten days it should be replaced by mercurochrome 220 1:4000, or albargin 1:6000. When other pyogenic organisms are associated, irrigations of Chloramine T 1:5000, or oxycyanide/

oxycyanide of mercury 1:5000 are preferable, and as the urethritis subsides astringent solutions such as nizin 1:2000, or zinc sulphocarbonate 1:1000, are advocated for their beneficial effect in stimulating resolution of the inflammatory process. As soon as the acute inflammation has subsided and the urine has become clear massage of the prostate and vesicles is instituted, and repeated biweekly until prostate smears are free from micro-organisms and pus cells.

In cases of chronic prostatitis and vesiculitis the most important therapeutic measure we possess is massage. It is performed twice a week and is always followed by urethral irrigation. During a course of four to eight weeks the prostate and vesicles usually return to normal, and smears taken subsequent to massage, are free from bacteria and pus cells. In some resistant cases further massage is necessary, after a rest of two weeks. The passage of a posterior sound, and local applications of 1-2 silver nitrate to the posterior urethra by means of a Ultzmann syringe, promote drainage from the prostatic ducts, and assist in clearing up infection/

infection in the prostate. If the ejaculatory duct is occluded on either side, a fine Geraghty syringe is passed through the posterior urethroscope into the mouth of the occluded duct which is syringed with a solution of 1% silver nitrate. Hot hip baths and rectal suppositories are valuable in chronic cases.

The best results in acute, subacute, and chronic cases are obtained by treatment along these lines. In my series it was found unnecessary to have recourse to operative methods.

Diathermy applied to the prostate and vesicles is an adjuvant to treatment, of special value in chronic cases. It should be used in association with, and not in place of, prostatic and vesicular massage.

I have had no experience of treatment by vasotomy, vasopuncture, vesiculotomy, vesiculectomy, or Pregl's solution.

I believe that vasotomy, vasopuncture, vesiculotomy, and vesiculectomy, are unnecessary procedures, and are only justifiable in severe cases of chronic seminal vesiculitis, which resist treatment/

ment by other methods. The post-operative results of vasotomy and vasopuncture, in acute and subacute cases, are no better than those obtained by conservative measures; and it must be remembered that lavage of the vesicles will not influence concomitant infection of the prostate, which is invariably present. Sterility follows vasotomy in a small percentage of cases. Vasotomy permits of lavage being repeated, and on this account is preferable to vasopuncture.

Vesiculotomy and vesiculectomy should never be practised until other methods of treatment, including vasotomy, have failed. They are difficult and serious operations, that do not give consistently good results. Vesiculectomy is always, and vesiculotomy often, followed by sterility, without impotence.

It is impossible at present to draw conclusions as to the value of Pregl's solution in the eradication of infection in the seminal vesicles. The passage of a needle into the vesicles through the rectum is a dangerous procedure on account of the risk of introducing other micro-organisms and

treatment/

treatment by this method is not recommendéd.

b. FOCAL TREATMENT IN WOMEN.

Infection of the urethra, cervix uteri, uterine tubes, or Bartholinian glands may be present. In all cases it is essential to maintain strict cleanliness of the vulval surfaces, and when these are irritated by urethral, vaginal, or Bartholinian discharges, to apply soothing dressings of lead and opium. Hot antiseptic hip baths are taken twice a day whenever possible.

In urethritis the best results are obtained by irrigations. These should be stronger than those recommended for lavage of the male urethra. The most suitable solutions are potassium permanganate 1:6000, albargin 1:4000, and mercurochrome 220 1:2-4000, Chloramine T and oxycyanide of mercury 1:3000, are preferable if there is infection with other pyogenic bacteria, and as the inflammation subsides astringent zinc preparations, such as nizin 1:1000, and zinc sulphocarbonate 1:1000 are more useful. Local application of antiseptic solutions/

solutions to the urethra, and the introduction of medicated bougies into the urethra, cannot replace irrigation in the treatment of urethritis, but are useful adjuvants. The results following the application of diathermy to the urethra, are no better than those following treatment by lavage. When littritis and submucous infiltrations are present, the most successful treatment is by instrumentation. A straight bougie is passed, and the urethra massaged on it through the anterior vaginal wall, or suction of the urethra is carried out with the aid of Mill's female urethral bougie. In resistant cases the infection may be kept up by an associated trigonitis. If this condition is observed by urethroscopical examination, local applications of silver nitrate or picric acid solution (1%), through the tube of the urethroscope, will clear up the condition.

In cases of infection of the endocervix vaginal douching is inadvisable. Success follows local applications in the majority of cases. The most useful antiseptics in acute cases are picric acid 1% in aqueous solution or glycerine, mercurochrome/

chrome 220 10 to 20%, acriflavine ½%, 50% formaldehyde in glycerine, 10% lunosol and 10% neoprotosil. Glycerine is valuable for its hygroscopic properties. In chronic cervicitis stronger antiseptics such as picric acid 2% in spirit and iodised phenol are indicated, the latter is especially valuable for the local treatment of cervical erosions. Compound dermatol powder is dusted over the cervix and vagina, subsequent to topical therapy. In chronic cases that are not reacting to treatment glycerine tampons, applied to the cervix for twelve hours at a time, promote drainage from the gland ducts and tend to draw the infecting agents to the surface. For the same reason, suction with Mill's cervical bougie is valuable. Dilatation and curettage of the cervical canal sometimes employed in these cases, are liable to spread the infection and set up a pelvic cellulitis and are therefore contra-indicated. Diathermy is an adjuvant to treatment in chronic cervicitis.

During menstruation local treatment of the cervix is suspended and it is advisable to prescribe liq-sedans, one drachm in water thrice daily, for its sedative effect on the uterus. It diminishes

the/

the severity of the period and lessens the risk of extension of infection into the uterus.

TUBAL INFECTION.

In acute cases conservative treatment is advisable in the first instance in the hope that resolution with restoration of function may follow, or that the infection may subside sufficiently to render subsequent abdominal operation less dangerous. The majority of cases of pure gonococcal salpingitis do well without operation, but if there are signs of diffuse peritonitis, such as general rigidity of the abdominal wall, rapid pulse, and incessant vomiting, operation should be undertaken immediately. In cases of pyosalpinx, it is advisable to defer operation till the acute stage is over and the pus has become sterile.

If conservative treatment is decided upon the patient is put in the Fowler position, and hot fomentations are applied to the lower abdomen, and aspirim administered for the relief of pain. The bowels are freely purged, and the diet limited to fluids/

fluids. As soon as the acute stage has subsided, hot hip baths, hot vaginal douches, and the insertion of glycerine and ichythol tampons are valuable in promoting resolution.

In chronic cases in which infection cannot be completely eradicated by conservative treatment, including diathermy and vaccine or protein therapy, the tubes should be removed by operation.

BARTHOLINIAN INFECTION.

When complicated by arthritis, infection of the Bartholinian glands, whether acute, subacute, or chronic, should be treated by excision of the gland. When performing this operation it is important to dissect the whole of the gland and its capsule from the surrounding tissue. If this is possible without opening into the capsule, the cavity is swabbed with tincture of iodine, its walls brought together with deep cat-gut stitches, and the wound closed without drainage. If the capsule ruptures, or if it cannot be completely dissected from the surrounding tissue, and in all cases of abscess, the edges of the wound should be loosely approximated after/

after the cavity has been sterilized, and drainage established.

c. FOCAL TREATMENT IN CHILDREN.

(1) Conjunctivitis.

The importance of early and frequently applied treatment cannot be over-estimated. In the acute stage half-hourly lavage with warm alkaline boric or saline solution is essential; it prevents the accummulation of pus and minimizes the risk of corneal ulceration. The conjunctival surfaces are flooded with a few drops of 10% lunosol or neoprotosil, or Crooke's collosol argentum 1:2000, three or four times a day. These colloidal silver solutions are non-irritating and it is unnecessary to wash the conjunctiva after their application. As the inflammation subsides the irrigations may be given at longer intervals and the silver preparations are only instilled twice a day. In the resolving stages of the infection, healing is stimulated by irrigating with zinc solutions, such as nizin 1:2000, or zinc sulphocarbonate 1:2000, once, or twice a day. If, at any stage of the disease corneal involvement/

volvement is feared, stropine drops (½ to 1% solution) are instilled into the affected eye twice daily.

In all cases when the condition is unilateral, it is of the utmost importance to avoid infection of the other eye. The sound eye is covered with a Buller's shield, and colloidal silver drops instilled twice or three times during the day as a prophylactic measure.

(2) VULVO-VAGINITIS.

The essentials of treatment are frequent cleansing and powdering of the external genitals, bidaily antiseptic hot hip baths, vaginal irrigations and local antiseptic applications, and simultaneous treatment of associated urethritis. To obtain the best results it is advisable to charge the irrigating fluid every three or four days. In the acute stages any of the following are suitable solutions for lavage, mercurochrome 220 1:4000 to 1:2000, potassium permanganate 1:6000, 10% lunosol or neoprotosil, or ½% picric acid. Medicated/

Medicated pessaries containing picric acid ¼ to ½%, mercurochrome 2½ to 5%, or lunosol 2½ to 5%, or a paste containing mercurochrome, should be introduced into the vagina subsequent to lavage.

In spite of every precaution the condition may become chronic; signs and symptoms disappear, but gonococci are repeatedly found in vaginal smears. In these cases stronger solutions, such as 1 to 2% silver nitrate, or 1% picric acid, should be applied twice a week directly through a urethroscopic tube, to the vaginal mucose, and to the cervix uteri if it shows signs of involvement. In the interval between local applications, hot hip baths and irrigations with the milder preparations are continued once a day. On account of the tendency of the infecting organisms to reach the submucous tissue, and evade the action of antiseptics applied to the vaginal mucose, local measures should always be supplemented by vaccine therapy.

(3) ADJUVANT TREATMENT.

Vaccines are invaluable in the treatment of all stages of gonococcal arthritis. A polyvalent detoxicated stock vaccine is preferable to a non-detoxicated vaccine, because it is less toxic, and can be administered in larger doses. A detoxicated polyvalent vaccine is more efficient than an autogenous vaccine of the patient's infecting organisms, in acute and subacute cases; but in chronic cases with mixed infection, the latter is preferable. If it is possible to obtain an autogenous vaccine, it should be injected along with the detoxicated vaccine in all cases. In subacute cases that tend to resist vaccine therapy, the efficiency of the vaccine can be increased by interposing intramuscular injections of proteins, and chemotherapeutic substances, between successive doses. For this purpose either aolan 5-10cc, sulfarsenol 18-24ctgs., or contramine..25gms may be used. Arthigon, a polyvalent gonococcal vaccine containing urotropine, is valuable in these cases. In chronic gonococcal arthritis it is advisable to commence treatment with/

with a short, biweekly course of protein injections, using aolan, peptone, or sterile milk. This is followed by long continued therapy with a polyvalent detoxicated stock vaccine combined with an autogenous vaccine. In chronic cases vaccines are well tolerated, and give better results if administered intravenously.

SUMMARY/

S U M M A R Y.

(1). Out of 4000 cases of gonorrhoea that have been reviewed, arthritis was a complication in 119. It was more common in men than in women (4:1); and it was more often poly-articular than monarticular. (5:1)

(2). The common sites of infection were the prostate and the seminal vesicles in men; in women they were the cervix uteri, the urethra, the Bartholinian glands, and the uterine tubes.

(3). The joint most frequently involved was the knee (64%); the others are named in their order of frequency - ankle, metatarso - phalangeal, shoulder, wrist, metacarpo - phalangeal, elbow, hip, inter-vertebral and mandibular.

(4). The signs and symptons of gonococcal arthritis are/

are analysed.

(5). It is shown that -

a. In diagnostic procedure thorough examination of the lower genito-urinary tract is essential;

b. the complement-fixation test, when positive, is diagnostic of gonorrhoea, and is of special value in those cases in which bacteriological evidence is lacking;

c. radiograms of the affected joints are of no positive diagnostic aid, but their negative evidence is sometimes of value.

(6). A critical review of the various methods of treatment is attempted, and the importance of treating the primary infection is emphasised.

(7). In acute and subacute cases, the prognosis is always good under suitable treatment - both local, focal, and general. In chronic cases the prognosis is unfavourable, and varies directly with the degree of involvement of the intra - and periarticular structures.

I wish to express my thanks to Mr DAVID LEES, D.S.O., M.B., F.R.C.S., (Edin.) M.R.C.P. (Edin.) for the facilities given for studying the cases reviewed in this Thesis.

I beg to state that the work has been done and the Thesis composed by myself.

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